A Peer Reviewed Quarterly Scientific Journal of Surgical Art, Science and Education

Archives of Surgical Research

## Bringing Surgical Science and Art Closer

Editor in Chief
Prof Khawaja M Azim FRCS

Archives of Surgical Research (ASR) is a double blind peer-reviewed quarterly ICMJE and COPE compliant journal dedicated to the local, national, and global advancement of surgical research, education and clinical practice. It aims to promote continued development in surgery through the dissemination of knowledge, ideas and good practice across surgical specialties. ASR provides readers with critically peer-reviewed, carefully selected and edited, and up-to-date publications about advancements in all surgery specialties.
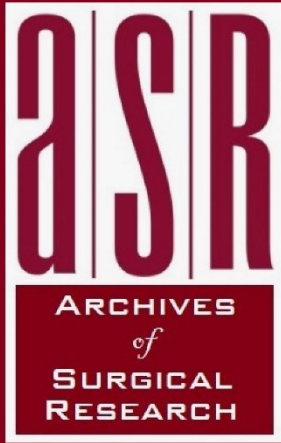
Archives of
Surgical Research
A Peer Reviewed Journal of Surgical Research & Education

ARCHIVES of SURGICAL RESEARCH

Editor in Chief: Prof Khwaja M Azim FRCS

About Archives of Surgical Research

Archives of Surgical Research (ASR) is dedicated to the local, national, and global advancement of surgical research, education and clinical practice. It aims to promote continued development in surgery through the dissemination of knowledge, ideas and good practice across surgical specialties. ASR provides readers with critically peer-reviewed, carefully selected and edited, and up-to-date publications about advancements in all surgery specialties.

The journal aims to uphold the highest standards at the cutting-edge of research, provide a focus for evidence-based medicine through the publication of review articles and special issues, and give the findings context through the publication of editorials, commentaries and letters from the surgical community. We ensure enforcement of reporting guidelines and mandate the registration of all research involving human participants in a publicly accessible research registry.

As a journal covering all surgical specialties, ASR aims to facilitate the transfer of important ideas and thought systems between and across specialties. Hence, ASR will help prevent the trend of increasing sub-specialization which leads to 'tunnel-vision' and the unfortunate concealment of important surgical advances within specific specialties.

Editor in Chief

KMA

Editorial Team

PREFACE

Shalamar Medical & Dental College has exceptionally excelled in the field of science, education and research over the last decade and has produced quality graduates who are currently serving around the world. Quality of education and research in surgery has been instrumental in this regard under the leadership of Prof Khawaja Muhammad Azim to achieve our core objective of producing quality education. Inception of Pakistan Endocrine & Thyroid Surgeons Association (PETSA) has aligned well to my vision, institutional requirements and overall rapport of the institution.

I witnessed and supported the birth of Pakistan Endocrine & Thyroid Surgeons Association here at Shalamar Medical College three years back and during this period it has evolved into a mature tree and is bearing fruits to surgical education and training here at our institution. Legacy of its founding visionary, Late Prof Syed Zafar Haider has continued. PETSA has been conducting Annual Thyroid & Parathyroid Master Class since its inception with great reception. Currently, we are the largest endocrine surgery center in Pakistan with highest volume turnover.

Now the introduction of "Archives of Surgical Research" is another feather into our institutions' cap. This journal would not only satisfy the needs of the society but would also serve to promote culture of science, education and research within our institution. This culture advocacy remains instrumental in promoting the quality of learning process of the medical graduates within our institute and is aligned with my vision about this medical college.

In the end, I am happy to write about "Archives of Surgical Research" and its inaugural issue and wish the editorial team best of luck for their endeavors for years to come.

Prof Zahid Bashir

Principal

Shalamar Medical & Dental College, Lahore

MESSAGE FROM THE PRESIDENT

Pakistan Endocrine & Thyroid Surgeons Association (PETSA)

Prof Zafar Haider was the teachers of the teachers and a great surgeon. He was the one who made thyroid and endocrine surgery safe in Pakistan and we carry the light now with aim to improve the endocrine surgery in light of modernization in the field of the surgery.

Archives of Surgical Research aims at improving the standard of surgical research and education. It would function as official Journal of Pakistan Endocrine & Thyroid Surgeons Association (PETSA).

The journal would cover endocrine, breast and surgical oncology primarily. It would also focus on the surgical education for medical students and residents to enhance the learning process through addition of technology, blended learning and modern concepts in medical education.

Prof. Khwaja M Azim FRCS
President PETSA

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Archives of Surgical Research | Perspective

Apprenticeship Model in 21st Century's Surgical Education: Should it Perish?

Saadia Shahzad, Muhammad Idrees Anwar

IMPORTANCE Traditionally the Apprenticeship has remained the backbone of any surgical training model for decades. This model ensures optimal surgical training quality by ensuring optimal trainer-trainee relationship and adequate exposure to the disease and operative spectrum. In this 21st century, both the quality of meaningful trainer-trainee interaction and operative or clinical exposure has come at stake due to multiple factors. These factors include rapidly advancing technology, more residents, the evolution of subspecialties, reducing working hours, and many others, which greatly compromise the strength and quality of apprenticeship. Keeping in view the strengths and benefits, and also identifying the need in the 21st century this model needs reincarnation. Newer pursuits like Proficiency-Based Progression (PBP) through Osler and Halstedian Model, quality assured assessment, use of simulated settings, augmented reality, and robotics are few choices. A carefully planned incorporation of strategies into these newer learning models is pivotal to maintain the essence of apprenticeship for not only keeping this model alive but also ensuring the quality of meaningful trainer-trainee interaction and adequate clinical exposure in surgical training.

KEYWORDS Surgical Training, Apprenticeship Model, Medical Education, Residents, Trainees

Perspective

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Dr. Saadia Shahzad, Department of Community Medicine, Shalamar Medical and Dental College, Lahore
saadiazahur@live.com
092-321-4767918
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Surgical training, traditionally, has remained more challenging, as the trainers not only have to impart on the clinical decision making and soft skills but also to the technical and motor skill realm. Going back in the history of surgical education it is very clear that since its inception, surgical education and training have undergone marked evolution. The initial attempt to improve surgical education was made in 1210 when in France clear differentiation and distinction was made between the 'academic surgeons' and 'barber surgeons'; where the first category was to be labeled so based on previous relevant university training in this regard. As a result, specified to the first category of academic surgeons 'The College de Saint Come' was established to systematically and methodically train the barbers in surgery[1]. For decades, the training has been my "role modeling' however the very first model of surgical training adopted, developed, and introduced in the 19th century is the 'apprenticeship model'. This method of training is ideally used to start at the age of 12-13 years and it would usually take 5-7 years of training for the students to become skilled surgeon[2]. The students were supposed to learn surgical skills through direct observation of their mentor and were then meant to replicate the same skills in a similar environment of an operating room (OR). The application of the apprenticeship model significantly improved surgical education, as an experienced mentor instructed the trainee, shared collective knowledge, and taught the surgical skill by demonstration, repetition, and scaffolding. The

apprenticeship model also promoted the "cult of the individual," with the development of masters who helped in developing competing "schools of surgery".

This model over many decades produced reliable training outcomes; however, few important challenges did emerge over some time. The major drawback was that it lacked structured programs available as to what skills were needed to be taught. It was based more on subjectivity and opportunity. Also less clear was the fact that for how long the training period should be? Who would be the eligible student for this training? [2]

Impressed by the German way of surgical training, William Halsted was the first to propose and implement a more robust structured way of surgical training at Johns Hopkins at the start of this century. Halstedian Residency training model soon gained support and, in 1928, the American Medical Association House of Delegates approved the application of this model in a more generalized way[3]. This model was based on the principle of 'see one, do one and teach one. It worked on the premise that acquiring increased responsibility by the surgical students' entails their becoming near-independent in the field of surgery. This model has successfully produced quality surgeons, teachers, and leaders in the field of a surgery over the last century[3]. Many developing countries still rely on this model of surgical training or a variant of it. Hence, Dr. Halsted is still

considered the father of modern structured clinical training in surgery

Halstedian model did not abrogate the apprenticeship model in principle but provided a structure and standardization to it. The master and the mentor still holds the key position in training and resident modeling. Over the past century, the Halstedian approach has evolved into Osler and Mall's competency-based progression in surgical training. These models have effectively produced well standardized, competent, and finest surgeons, who have performed brilliantly in American as well as international perspectives and still prevalent in many training programs.

However, over time, the need for more advanced techniques kept evolving that could give enhanced safety and training structure. There was a very obvious limitation that was being overlooked for a long time in apprenticeship and Halsted model and that was: 'to err is human' according to the landmark report of Institute of Medicine in 1999; stating the fact that each year around 44000 – 98000 patients in the hospitals of USA die due to preventable medical errors[4]. Evidence suggests that trainee doctors are responsible for most prescribing errors[5]. The report also challenged the patient safety factor of the patients while students were trained by these models, and so alternative methods of surgical training and teaching were started gaining attention[4]. Another reason for shifting was the higher cost of training surgical residents in OR with the mentor[6]. Therefore, teaching surgical skills outside OR with the added benefit of enhanced patient safety, less stressful teaching environment; led to the foundation of virtual simulated-based training in surgical education[7]. This innovative model enables a surgical trainee to learn and practice minimally invasive surgery on synthetic models, animals, or cadavers; in virtual and augmented reality[8]. The quality of training in a simulated environment, however, remains inferior to real-life training opportunities. Advances in Minimally Invasive Surgery (MIS) and Robotic Surgery are pushing us to rely more on the simulated setting, virtual reality, and augmented reality to teach decision making and motor skills in a safer environment, which certainly has advantages and has proven to be beneficial for the surgical training. Few, however, fear losing adequate attention to clinical exposure and real-life operative exposure which have remained instrumental in making great surgeons in past.

Recently during the last couple of decades, the development of soft skills in surgeons has gained attention. Technological advancement, higher expectations of the stakeholders in health care, skyrocketing health care cost, and enhanced awareness on part of the patient; has led to the fact that besides a modernized and enhanced skill training program, soft skills of the surgical trainees must also be developed well, to ensure the satisfaction of the stakeholders in health care. The Royal College of Edinburgh labels these as non-technical skills in surgery (NOTSS) which can be broken down as skills and behavior, situational awareness, decision making, communication skills, teamwork, and leadership behavior[9]. It's now long proven that errors in the surgical field occur not only because of technical faults, but these soft non-technical skills also have a major role to play in certain situations[10].

You will all agree that now the training of surgery is not as robust as it used to be [11]. This could be attributed to changes in the training models, gradual shift to simulated settings, rising number of surgical trainees, training hour restrictions, ethical issues, and fewer operative opportunities. These have started eroding this interaction and thus the quality of resident training. This whole narrated context is tinkling my mind towards a query if apprenticeship model is not able to cope up with the evolving need for surgical education? How the basics of apprenticeship would hold in this changing training environment? Is the apprenticeship model of surgical training taking some last breaths? Is it perishing?

The authors' opinion "It's not!"

There is a uniform consensus among the surgical teachers that a meaningful trainee-trainer relationship, harmony, and interaction remains key to quality surgical training. Many components of the apprenticeship training model are still applicable in this day and the overarching umbrella principle of apprenticeship with its progressive step-by-step transfer of patient care responsibilities; with hierarchical autonomy in the OR, is still the main focal point in surgery training program. I would argue in favor of keeping the soul of the apprenticeship model alive in our newer training models and realms. A careful balance needs to be carved between the virtual realities / simulated setting-based curricula and real-life operative experience.

Why apprenticeship model still needs to live? My premises for this counter-argument are:

- Results of the apprenticeship model have consistently proven to be good in producing skill competency in surgical residents and interns.
- Advanced & complicated surgical skill-set training is more effective through apprenticeship, rather than by virtual reality. Clinical methods, clinical judgment, and rationalized clinical decision-making can ideally be taught by this model.
- Role modeling element of apprenticeship model is crucial for imparting affective domain training. The mentor, as a role model, is more effective in training soft skills (behaviorism & communication skills) to the students as compared to the virtual simulated technology;
- Emotional training and intelligence like keeping calm & composed in an emergency or, dealing with disruptive patients can be taught best by this model;

long-lasting mentor-mentee relation; & empathy is best taught by the apprenticeship model.

The authors suggest:

1. Adequacy of quality clinical and operative exposure and trainer-trainee interaction, which is the essence of the apprenticeship model, should remain an important component of any surgical curricular design. The trainer-trainee ratio, patient volume, and operative procedures performed under the supervision and independently should be standardized and competency-based quality assured.

2. Regular trainer's training programs, which can fulfill the role and responsibility of Mentor/Role model in the overarching umbrella of the apprenticeship model can be used to enhance the number of surgical residents and training.

There is no need for the apprenticeship model to bow out on the stage of surgical education! This is and would remain the backbone of any surgical training model. This model will fight back and will not perish.

Author Affiliations. Dr. Saadia Shahzad, Department of Community Medicine Shalamar Medical and Dental College, Lahore; Prof Idrees Anwar FRCS, DCPS, HPE (CPSP), MHPE(KMU) is Dean Department of Surgery and Allied at Rawalpindi Medical University, Pakistan.

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Archives of Surgical Research | Original Research Communication

Barriers To Early Presentation Of Symptomatic Breast Cancer In Local Population: A Qualitative Study

Maira Dastgir Nousherwani, Hira Tariq, Talat Waseem

IMPORTANCE Breast cancer is the most common type of cancer in women and the second most common after lung cancer in the world. Statistics consistent with GLOBOCAN 2012 state that 1.67 million cases of breast cancer were diagnosed in 2012 alone and resulted in 522,000 deaths that year making it the most frequent cause of cancer death in women in less developed regions. Pakistan itself has the highest prevalence of breast cancer amongst all countries in Asia where every one-in-nine women are likely to suffer from it at any point in their lives. In addition to the high disease burden, a major fraction of these cases is diagnosed at advanced stages. This advanced stage diagnosis results in more aggressive treatment, poorer outcomes, poorer quality of life and higher mortality rate. Public awareness of this disease may help in early detection of breast cancer, decreasing mortality rates and, ultimately, increasing probability of survival. Identification of these delaying factors is crucial for removal of barriers to early detection and treatment of breast cancer patients.

METHODS This is a qualitative study based on interviews and includes breast cancer patients as study participants. 24 Subjects fulfilling the inclusion criteria were selected from Shalamar Hospital's one stop Breast Clinic data by purposeful criterion I sampling and their consent was taken for an in-depth interview according to a preformed interview-guide, taking 20-30 mins each, which were then transcribed. Transcribed interviews were further managed using QSR NVivo (V. 9). Iterative analysis following tenets of grounded theory identified themes and their inter-relationships. Thematic analysis was undertaken, and final results explained in tables and percentages.

RESULTS Twenty-four women were included in this study, four women had passed away due to severity of their disease, four women did not agree to become a part of our study and there were sixteen women who consented for it. All sixteen women were aged >40 years and were married. Several barriers to early presentation and diagnosis of Breast Cancer were reported and identified.

CONCLUSIONS A significant percentage of women with breast cancer in Pakistan delay presentation primarily because of lack of awareness about the disease and its management. Along with the need to be examined by female doctors only, failure to understand breast cancer symptoms, ignoring them, and reliance on spiritual healers for cure were all identified as significant risk factors for delayed presentation. Coordinated efforts are, therefore, needed from public health departments regarding awareness about breast cancer and its therapeutic outcomes, to educate women and remove the barriers identified.

KEYWORDS Breast Cancer, Early Identification, Barriers, Prognosis

Qualitative Study

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author:
Talat Waseem FRCS Eng, FACS
Department of Surgery,
Shalamar Medical & Dental College, Lahore, Pakistan
twaseem@gmail.com
092-333-8078705
https://doi.org/10.48111/2021.03.02

B reast cancer is the most common type of cancer in women and the second most common after lung cancer in the entire world[1]. Statistics consistent with GLOBOCAN 2012 state that 1.67 million cases of breast cancer were diagnosed in 2012 alone and resulted in 522,000 deaths that year making it the most frequent cause of cancer deaths in women in less developed regions[2,1]. Between 1975 and 1990, Asia and Africa experienced a more rapid rise in the annual incidence rates of breast cancer than North America and Europe[3]. Pakistan itself has the highest prevalence of breast cancer amongst all countries in Asia where every one-in-nine women are likely to suffer from this disease at any point in their lives [4,5]. Approximately 90000 new cases are diagnosed every year out of which 40000 pass away[6]. A study on the incidence and mortality of breast cancer demonstrated that the highest age standardized death rate (2.52) in Asia due to breast cancer was observed in Pakistan [7].

In addition to the high disease burden, a major fraction of these cases are diagnosed at advanced stages. A study

reported how a high proportion of breast cancer patients [around 71% of the cases at INMOL and 63% at SKMCH (Local Cancer Hospitals)] presented to their Breast Clinics at stages III and IV [8]. Such a late presentation points to the alarming situation of the rising trend of breast cancer incidence in Pakistan. This advanced stage diagnosis results in more aggressive treatment, poorer outcomes, poorer quality of life and higher mortality rate [9]. Public awareness of this disease may help in early detection of breast cancer, decreasing mortality and, ultimately, increasing the probability of survival. The average 5-year survival rate for women with non-metastatic invasive breast cancer is 91%. The average 10-year survival rate for women with invasive breast cancer is 84%[10]. If the invasive cancer is located only in the breast, the 5-year survival rate of women with breast cancer is 99%[10].

This delayed presentation may be related to diverse factors, including women's lack of knowledge about the disease, methods to diagnose early and various cultural factors. This highlights the need for mechanisms that can help detect this cancer early and even treat it early. The duration of delay in seeking medical aid after the appearance of breast cancer symptoms can be reduced by identifying possible factors contributing to the delay which could improve early diagnosis of the disease at a less advanced stage. This would lead to better prognosis and, ultimately, improved survival rates in Pakistan[11].

Several studies have reported multiple factors responsible for advanced stage presentation. There is a lack of awareness about symptoms and importance of self-breast examination[12]. Patients are often unable to relate their initial symptoms to Breast Cancer unless they were lump-related symptoms[13]. Low socioeconomic status has been seen to be linked with advanced stage presentation and worse outcomes [14]. Educational status, awareness about disease and access to health care resources are regarded as significant factors in this regard [15]. All these factors can broadly be classified as personal, sociocultural and economic barriers.

This study was designed to identify barriers by analyzing patients' perceptions and factors involved in delayed breast cancer presentation in the local cohort of the population through qualitative methods crucial for removal of the barriers for early detection and treatment. Eventual aim of this study is to target the barriers identified by addressing them through goal directed specific mass media and other awareness campaigns in Pakistan.

METHODOLOGY:

This is a cross sectional qualitative study carried out from May 2020 to December 2020 at Shalamar Hospital which is a not-for-profit 500 bedded tertiary care hospital in Lahore. The study was based on in-depth interviews and included breast cancer patients presenting to Shalamar Hospital's One Stop Breast Clinic as study participants. Fifty women who had presented to Outpatient department from 2019

June to 2020 May were randomly selected from the available data. The sampling technique then applied was Purposeful – Criterion I. Twenty-four participants were selected for the study (of 18 years and above) that had presented with breast-related complaints of two months or more, had breast carcinoma and if their lesions were not screen detected. Principal investigators conducted 1-on-1 in-depth interviews through a guide after consent was taken from the study population. Twenty-four women were contacted out of which three had already passed away owing to their aggressive malignant diagnosis and remaining five did not consent to become a part of the study. The research instrument consisted of a specially developed questionnaire-guide in English and Urdu language. It contained open and closed ended questions related to the respondent's knowledge, awareness regarding breast cancer, screening techniques, economic and social reasons affecting early presentation to Outpatient department etc. The guide allowed study participants to talk about salient themes in their own words at their own pace. Each interview took 20-30 minutes and was recorded. They were transcribed with the help of QSR N-vivo (V.9). Researchers went through transcripts line-by-line to categorize and describe data, and then developed themes through selective and conceptual coding e.g. IIIB5 (257), where III= participant, B= theme, 5=subpart, 257=line number. Newer themes were made a part of subsequent interviews. Iterative analysis following tenets of grounded theory identified themes and their inter-relationships. Thematic analysis was undertaken, and final results explained in tables and percentages. The interview guide is attached at the end of the article as appendix I.

Study design and questionnaire were evaluated and approved by the Institutional Ethical Review Committee Board of Shalamar Institute of Health Sciences, Lahore, Punjab (reference number SMDC-IRB/OL/025-2019). The entire study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from each patient to access their medical records along with authorization to use personal/genomic data for publication.

RESULTS

Study Characteristics: A total of fifty women were contacted out of which 24 fulfilled our inclusion criteria, leading to a sample size of twenty-four. Out of these twenty-four, four had passed away due to severity of their disease, another four did not agree to become a part of our study and sixteen women consented. All sixteen women were aged >40 years and were married. Several barriers to early presentation and diagnosis of Breast Cancer were reported and identified. Table 1 shows the summary of barriers to late presentation of Breast Cancer reported in this study including respondents' personal reasons and perceptions for late presentation or diagnosis of Breast Cancer. Supplementary material includes Table 2 and Table 3

containing themes and subthemes formed respectively. Transcription of 16 interviews is also included.

Lack of knowledge about cancer: Out of the 16 participants, 10 were seen to lack knowledge about the cancer in general, its types, treatments, signs, symptoms and risk factors. 2 of them claimed to have never heard its name before. Most of these women did not have enough information even after contracting the disease themselves. The rest of the women had a fair idea that cancer was a fatal disease and that its treatment constituted of getting operated upon.
"I had never heard the name of the cancer till it happened to me. I never believed it could be something so serious."

Lack of knowledge about breast cancer: When specifically asked about breast cancer, 7 of the participants lacked proper information about the disease while the other 8 had some idea about it because of previously diagnosed cases in their families and relatives. *"As I said, I didn't know anything until I became its prey. By the way I've heard that women who don't breastfeed their children and who keep their phones near their chests are at increased risk (to develop cancer of breast)"*
Since this section included open ended questions, women went on to say, *"In my opinion, it (breast) is a relatively safe area for a cancer to occur as the whole of the breast can be removed without significantly affecting on one's life".* In addition, whatever little information they learned of was from their own experiences as well. *"All I know about breast cancer is from my own experience. Otherwise, I had no prior knowledge about it."*

Lack of awareness about self-breast examination: Only 2 of the participants knew what self-breast examination was, while the rest had no information about it. While one said, *"I don't know how to self-examine the breast. But I want to learn and also want my daughters to learn it."* Another stated, *"I am not aware of any of the methods used to know about cancer before its manifestations. I wish there was a way of knowing this earlier. I wouldn't have gone through so much pain."*
In contrast to these statements, the rest of our participants had different answers. While one responded, *"I don't have any idea about methods used to make early diagnosis of cancer",* second participant said, *"I never paid any attention to such processes. I don't know what breast examination is about";* interestingly so she went on and completed her answer by saying, *"I don't think so my doctor told me about any self-examination".*

Lack of awareness about screening: Thirteen of the participants, when asked about screening, were not aware of the screening methods available. Most of the women had not even heard the name of "screening" before. *"Screening? I don't know. I underwent many tests like bone scan etc. I don't know exactly if these are the screening methods you are asking about."* Our participants even lacked basic

information being showcased through our mass media awareness campaigns as majority of them were unaware of what pink ribbon was or what the annual breast cancer awareness day was. *"I have seen Pink ribbon at various places but I don't know what it is".* The most known screening method owing to their own experiences was "mammography" and "biopsy". One stated, *"There are some tests which are performed annually to identify the disease before appearance of the symptoms, I know about mammography."* Another responded, *"...I got FNAC done, I was told my treatment would be decided on its basis"*

Culture and religion as barrier: Culture and religion proved to be a barrier for 3 of our participants only. One of our subjects claimed that she visited a spiritual healer before going to a doctor. She explained, *"I went to a spiritual healer, he did Dum (Bless with the word of God) on me. My pain got better and the swelling (in my breast) changed its size (decreased)."* The remaining 13 women had strong religious values but it did not prove to be a hindrance in early presentation. These women believed that this disease was given by God and God alone would provide cure for it.

"I am a Muslim. Every disease has a cure and the cure lies in the Quran. Other than that, seeking a lot of forgiveness if you think you have wronged yourself and be patient and persevering in facing this trial can help you battle this disease. In Islam there is no halal or haram thing when it comes to saving life".

Economic issues as a barrier: Even though almost everyone agreed upon the fact that financial conditions affect visiting doctors in countries like Pakistan, only 2 of our participants were unable to present early due to this specific issue. Representative statements are as follows, *"Postoperative treatment like chemotherapy and Herceptin injections is really expensive. Poor people can't afford this and this leads to poor compliance with treatment procedures"* and *"There was a neighbor of ours who died from not affording the treatment expenses. But Alhamdulillah (praise be to God) I didn't face this (financial) problem".*

One of the subjects thought, *"Many of our government hospitals are providing treatments that are affordable for the poor as well".* Another added, *"I think it (money) plays a positive role in early presentation but my case was different".*

Educational status as a barrier: In 20.8% of the women, educational status was linked to their delayed presentation. Majority of the women had studied till secondary school only and did not perceive their education to have played a role in this regard.
"No. Even if I was educated, I would have only gone to the doctor if I had discomfort (in my breast) like this time."
While some were of the opinion that *"It (education) plays a pivotal role",* 4 of the participants stated in similar wordings, *"I don't think education has a role in early presentation as*

everybody should be wise enough to know about importance of self-care". Education was perceived as largely unrelated to presenting late.

Lack of facilities as a barrier: 3 women presented late due to lack of availability of diagnostic and treatment facilities. In their opinion, hospitals were not well equipped to treat suffering patients. The other 13 did not face any difficulty in this regard.
"They (facilities) have been improved to some extent now. But 2 years back, when I was undergoing treatment, the hospitals were in much worse condition. But still there are a lot of things to improve especially in public sector hospitals."
"I think the facilities are satisfactory. The responsibility lies on the shoulders of both the doctors to make a correct and timely diagnosis and the patients to stop taking their symptoms for granted."

Lack of human expertise as a barrier: According to 4 women, it was lack of human expertise that led to their delayed presentation. The perception of lack of human expertise resulted from misdiagnosis from a doctor that led to eventual delay in presentation. *"I don't know what to say about this? The first doctor to whom I went misdiagnosed me but it didn't end here. My symptoms were getting aggressive by each passing day..."*

The other 12 were relatively satisfied with their treatment. All of them commended the abilities of their surgeons and clinic staff. *"They treated me very well. They were quick in diagnosing my condition correctly and provided me with good treatment."*

Ashamed of being examined by a male doctor: Seven women stated that the scarcity of female surgeons was somewhat responsible for delayed presentation. They described the experience with male doctors to be uncomfortable and awkward.
"The biggest problem of our health setup is that lady doctors are very few. It is a source of huge embarrassment to expose ourselves in front of male doctors." The rest were unclear if they thought this was a barrier as they said, *"it was a matter of life and death...",* an absolute necessity so they didn't let shame come in their way. One respondent, however, reported that "*In general, female doctors are majorly gynecologists and less are surgeons. Male surgeons are more common so it doesn't leave us with many options anyway."*

Insufficiency on media's behalf: 37.5% women believed that the media is not doing enough to educate women about this disease. 16.66% seemed to be satisfied with the efforts of the media in this regard. Their main concerns were collectively targeted towards broadcast media; that it should showcase more programs about breast cancer. The others refrained from giving any statement since they did not have access to social media and television.

"No there are not enough programs running on the media to educate women about it. And if there are any, they do not discuss it openly."

"Media is not projecting this issue effectively. How I know that something like breast cancer exists is by being able to see people suffering from this disease around me. I haven't seen any information in newspapers or TV."

Lack of family support/social pressure: Lack of family support was not seen to be a major factor in delayed presentation: only 1 woman faced this problem.
"It is important for families to support their women in these times and my family especially husband did whatever he could for my treatment."

Fifteen of our participants received full emotional and social support from their family members including their husbands who were termed as major support systems. One of them added, *"I have an extended family but nobody changed their attitude towards me. They were supportive throughout. However, in most of the cases, it is the joint family system which makes things difficult for women. There is a continuous pressure, more responsibilities and more financial issues to deal with."*

Failure on doctors' part in effectively educating patients: According to a few of our participants, their doctors did not provide them with enough information about their disease. This was a common answer when asked about screening methods and about Breast Self-examination. One participant said, *"I don't think so my doctor told me about any self-examination."* On the other hand, 13 subjects were of similar views that, *"Whatever information I have, I got this from my doctor".*

Lack of information transference by the patients: Three of our participants believed that it was the lack of transference of knowledge and sharing of experience by the patients, which contributed to late presentation. It was believed that the information coming from the patient herself is easier to believe and act upon.

"I think the patients should also educate the other women and share their experiences. As the information coming from the patients themselves is more accurate and acceptable by the society." When asked if they transferred their information to others in order to overcome the barrier that they felt, a respondent claimed that after she had shared details of her diagnosis and ongoing treatment with her cousin, it resulted in latter getting diagnosed with breast cancer as well. (line 1877, participant XVI)

Perceiving early diagnosis unimportant:
According to 4 participants, early diagnosis had nothing to do with prognosis: early or late presentation did not make

any difference in their view. Some of them attributed this to God giving this disease when He wills. *"Allah gives everything and only he has the power to take away anything".* Twelve women believed it to be an important factor in determining the survival of the patient.

"Yes, the earlier we know, the better it is. The delay in diagnosis is associated with decreased survival chances as the disease is untreatable at late stages"

Lack of facilities in smaller cities: 3 participants believed that there were disparities between the health care facilities in smaller and larger cities. People living in smaller cities do not have access to latest diagnostic techniques and the doctors are not as competent as those in big cities. Consequently, they may have to travel to bigger cities or suffer at hands of ill-equipped hospitals.

"There is an extreme mismanagement in hospital settings and lack of facilities especially in smaller cities. I am from Sahiwal and the hospitals there are really small. I think we should open more breast clinics and make treatment for breast cancer more accessible for all the people"

Ignorant attitude of patient towards their disease: Eight participants agreed that their ignorant attitude towards their symptoms became responsible for their delay. Deliberately ignoring the symptoms when they occur proved to be the main reason behind their delayed diagnosis. *"I think had I not ignored it, and just gone to the doctor when I first noticed it, my diagnosis would've been made on time. I regret ignoring it"* She goes on: *"I told my husband but we ignored initially as we got scared and many superstitions crossed our minds and we kept on thinking what we should do about it. But actually, did nothing"*

Prioritizing spiritual healers over doctors: In Pakistan, the concept of spiritual healing is prevalent. Out of 16, 4 participants preferred going first to spiritual healers instead of seeking medical help consequently presenting to medical centers late. Majority were of the view,

"I believe doctors should be trusted as they are extremely competent, they spend years studying and then become someone who can serve humanity. They know what they are doing"

The rest even though did not visit any spiritual healer, they did believe in, *"... getting better by reciting Quranic Verses."*

Fear of death: According to one participant, fear of death also withholds women to seek medical attention. They do not want to face reality and decide it is better to stay silent.

DISCUSSION

Early stage of diagnosis is a key determining factor for survival of breast cancer patients, and delays in diagnosis and advanced stage of presentation are associated with poor clinical outcomes [16,17].

This study provides critical insights into why women delay in seeking care for breast cancer symptoms; the most important and recognized ones being a lump in breasts, discharge from the nipple, pain/soreness, skin puckering or dimpling; and a change in breast shape[18].

Apart from confirming themes that have been elucidated via preceding researches, this study provides clarification and an in-depth explanation for the role played by lack of knowledge, religious beliefs and monetary limitations that contribute to delayed breast cancer presentation. Our results show that lack of awareness and lack of education are key factors contributing to late presentation for breast cancer patients. Several capacity issues of health-care providers were also identified.

A major patient related-barrier to seeking early medical care was lack of knowledge which lead to patients attributing different meanings and superstitions to their symptoms and were, therefore, unable to recognize these symptoms as something serious. This ignorance caused women to present at advanced stages (III and IV) of their disease in countries like Pakistan [8]. This is consistent with findings from an Ethiopian study that revealed how patients let the symptoms take their natural course without seeking early medical care[19], which is in sharp contrast to the international literature from first world countries where only 10% or fewer women had a metastatic stage (i.e. stage IV) of breast cancer at presentation[20]. Cultural barriers caused married women to have less access to caregivers and poor orientation towards attending targeted health units alone because they were dependent on their husbands or heads of the family[21]. All of the participants in this study were married and, hence, relied on family support. All study participants stated that they had complete support from their families and did not perceive this as a barrier. They, however, did believe the scenario would be different had this support not been present. This is consistent with a South African study reporting that 20.7% of their study population needed permission from spouses in seeking healthcare[22]. As is commonly reported in many cultures, married women often have domestic responsibilities[23]. Likewise, the responsibilities of women in African culture make health a low priority and prevents them from seeking healthcare and/or attending educational forums[22].

Majority of patients described their reluctance to get examined by male doctors. They shared this perception in consistence with African studies that explain how it was not culturally acceptable for women to show their breast(s) to another male except the husband[19]. 2/3rd of our participants explained the need to have more female doctors so that patients could be comfortable with the diagnostic and treatment process.

Themes		Total =24	%	Representative statements
Lack of knowledge about cancer as a barrier	Yes	10	41.66	"I had never heard the name of the cancer till it happened to me. I never believed it could be something so serious."
	No	6	25	"Cancer cells are healthy cells of our body which instead of dying start invading other cells of the body and disrupt their function."
	Unclear	0	0	
Subtheme: 1. Perceiving education irrelevant				"I don't think education has a role in early presentation of breast cancer. Everybody should be wise enough to know about the importance of self-care."
Lack of knowledge about breast cancer as a barrier	Yes	7	29.16	"As I told, I didn't know anything until I became its prey. By the way I've heard that women who don't breastfeed their children and who keep their phones near their chests are at increased risk"
	No	8	33.33	"I only know about one type of cancer and that is breast cancer. I know it's a disease of the cells of our body but I don't know about the details."
	Unclear	1	4.16	"I have heard that the women who don't breastfeed their child or keep their mobiles near their chest are at increased risk of this cancer."
Subthemes: 1. Insufficiency on media's behalf 2. Perceiving early diagnosis unimportant				"No, there are not enough programs running on the media to educate women about it. And if there are any, they do not discuss it openly." "No, there is no importance of knowing about it earlier. it is given by Allah and taken away by Allah. When he wants, he makes the person aware of it"
Lack of awareness about self-breast examination as a barrier	Yes	4	16.66	"I am not aware of any of the methods used to know about cancer before its manifestations. I wish there was a way of knowing this earlier. I wouldn't have gone through so much pain."
	No	2	8.33	"We should examine our breasts regularly. We should never ignore any pain, redness, feeling of lump and nipple changes as these are one of the signs of cancer."
	Unclear	0	0	
Subthemes: 1. Failure on doctors' part in effectively educating patients 2. Lack of interest of patients to know about their disease 3. Lack of information transference by the patients				"I don't think so my doctor told me about any self-examination." "I am an uneducated woman. This is related to your field. How can I know about it?" "I think the patients should also educate the other women and share their experiences. As the information coming from the patients themselves is more accurate and acceptable by the society."
Lack of awareness about screening as a barrier	Yes	13	54.16	"Screening? I don't know. I underwent many tests like bone scan etc. I don't know exactly if these are the screening methods you are asking about."
	No	3	12.5	"There are some tests which are performed annually to identify the disease before the appearance of the symptoms. I know about Mammography"
	Unclear	0	0	
Culture and religion as a barrier	Yes	3	12.5	"I went to a spiritual healer. What did he do? He did "Dum" on me (recited Holy Quran and blessed me. my pain got better and the swelling changed its size."
	No	12	50	"I am a Muslim and I think Allah wants us to take care of ourselves and let the doctors do their job"
	Unclear	1	4.16	"I didn't go to the Hakeem or spiritual healers but I did get "dum" (blessed by the verses of Quran). Why? Because I wanted to get satisfied that I had tried every avenue to get cured, I had to be sure"

Subthemes: 1. Prioritizing spiritual healers over doctors 2. Lack of social support/ family pressure 3. Reluctant to share with families 4. Ignorant attitude of patients as a barrier				"I went to the spiritual healers for at least six months. I used to feel fatigued and tired. I began to experience bloody discharge from my lump." "It is important for families to support their women in these times and my family especially husband did whatever he could for my treatment." "I think had I not ignored it, and just gone to the doctor when I first noticed it, my diagnosis 4) would've been made on time. I regret ignoring it"
Economic issues as a barrier	Yes	2	8.33	"Yes, money is really important. Money is life and death basically. Even though I have doctors in my family and I got treatment through a reference, this is a big factor in people like me presenting late."
	No	14	58.33	"There was a neighbor of ours who died for not affording the treatment expenses. But Alhamdulillah I didn't face this problem".
	Unclear	0	0	
Educational status as a barrier	Yes	5	20.83	"No. Even if I was educated, I would have only gone to the doctor if I had discomfort like this time."
	No	11	45.83	"I have studied till 8th standard. No, because as soon as I realized the problem, I knew I should consult a doctor which I did."
	Unclear	0	0	
Lack of facilities as a barrier	Yes	3	12.5	"They have been improved to some extent now. But 2 years back, when I was undergoing treatment, the hospitals were in much worse condition. But still there are a lot of things to improve especially in public sector hospitals."
	No	13	54.16	"I think the facilities are satisfactory. The responsibility lies on the shoulder of both the doctors to make a correct and timely diagnosis and the patients to stop taking for granted their symptoms."
	Unclear	0	0	
Subtheme: 1. Ashamed of being examined by a male doctor 2. Lack of facilities in smaller cities				"The biggest problem of our health setup is that lady doctors are very few. It is a source of huge embarrassment to expose ourselves in front of male doctors." "There is an extreme mismanagement in hospital settings and lack of facilities especially in smaller cities. I am from Sahiwal and the hospitals there are really small. I think we should open more breast clinics and make treatment for breast cancer more accessible for all the people"
Lack of resources and human expertise as a barrier	Yes	4	16.66	"I don't know what to say about this? The first doctor to whom I went misdiagnosed me but it didn't end here. My symptoms were getting aggressive by each passing day and I was being referred from one doctor to the other. Some claiming it to be an infection other arguing it to be a tumor."
	No	12	50	"They treated me very well. They were quick in diagnosing my condition correctly and provided me with the good treatment."
	Unclear	0	0	

Table 1: Summary of Qualitative Findings.

They reiterated feeling ashamed while getting examined by male doctors as the breasts are still viewed within similar cultural settings as symbols of womanhood, nurturing, and sexuality [24,25]. A large study from a representative sample of general practitioners in Manchester similarly reported that women doctors saw more women patients than men doctors for cervical smears, contraception, and breast disorders[26].

In a study conducted by Mitchel et al in North Carolina, United States of America, it was stated that a fraction of women believed medical treatment was unnecessary because only God could cure breast cancer[27]. Findings from our study suggest matching results as subjects outlined experiences where they preferred getting blessed by the word of God which in local language is known as "Dum" along with getting cured by spiritual healers. Padela et al's

investigation asserted that American Muslims with higher degrees of religiosity were less likely to have had a mammogram in the past 2 years[28].

Participants stated their diseases were adversaries sent by God and they could be treated only if God willed. A study in India revealed similar beliefs that cancer is caused by God's curse[29]. Thus, reliance on non-medical treatment is a significant barrier to early medical care. This is supported by claims that throughout Muslim history, Greco-Arab and Islamic herbal medicine were the first choice of treatment for ailments involving many other diseases as well as cancer[30].

Findings from several studies determined that women were reluctant to check their own breasts[31] and feel embarrassed when discussing breast-health concerns with others[32]. At a time when Breast self-examination (BSE) is the simplest and easiest mode to check one's self on monthly basis [8], lack of awareness regarding self-examination and screening methods proved to be one of the most important barriers since majority of our respondents did not know about BSE, screening methods or about breast cancer awareness days; if women were unaware of how their breasts normally functioned, they would consequently only detect changes when disease has relatively progressed.

In most studies, it is reported that most women received Breast Cancer information mainly from television (31%), clinics (31%), and health professionals (21%)[22]. This even though matches our results where majority women reported getting any/all information they had from hospitals and doctors, is discordant with our study stating there is insufficient coverage of breast cancer in Media, both broadcast and print. This laments the need for widespread media campaigns to help in spreading breast cancer awareness. A paper published about Breast Cancer in limited resource countries stated that the need for awareness programs in relation to early preventive strategies is obvious[33].

The work of Schneider along with many other studies demonstrates clearly the coexistence of socioeconomic factors' impact on cancer staging and outcomes[34]. While some studies showed participants with higher educational attainment were more knowledgeable about breast cancer issues than those with lower education attainment[35]. Others explained the large economic impact of breast cancer in lower and middle income countries presenting a financial burden making limited household income and health-care costs contributing factors to the delay in seeking help[36]. This is demonstrated by our results as well. Individual patients and households face significant out-of-pocket costs when seeking treatment in private setups as breast cancer or other health concerns are not considered a political priority.

Furthermore, lack of facilities in smaller cities which is additionally reported as a barrier in our study causing

patients to travel to bigger cities to get better medical treatment causing further delay. Therefore, it was observed that people living in third world countries often had limited healthcare infrastructure to provide adequate care and treatment for diseases including breast cancer[37]. The survival rates of BC are higher in countries like UK covering treatment costs [37]etc.

This leads to the observation that governments should focus on improving literacy and providing screening programs which will only prove to be cost-effective since early identification of disease is primarily treatable with a single treatment modality instead of a combined surgical and oncological treatment process. This will significantly lower any disease burden in Pakistan, especially that of Breast Cancer.

Among all the premenopausal and postmenopausal patients, the moderately dense category C mammographic density was observed in 70 (46.1%) patients, followed by high density category D mammographic density in 60 patients (39.5%). Similarly, minimal BPE was seen in 70 (46.1%) patients as depicted in table 2. The categories of MD were divided in low (category A and category B) and high (category C and D). The BPE categories were also divided into high (moderate and marked) and low grade (minimal and mild).

Limitations Our findings should be interpreted in light of the fact that the qualitative methodology has some limitations. The present study had a small sample size compared to the large number of breast cancer patients in the Pakistani population, and was limited to breast cancer patients who visited Shalamar hospital in Lahore. Therefore, there may have been a bias in the data related to the regional and socio-economic background characteristics of the patients. In addition to this, the study setting was greatly disturbed due to the Covid-19 pandemic. Interviews had to be conducted over telephone to observe social distancing and consequently were affected a great deal due to connectivity issues. Therefore, similar studies must be conducted in other hospitals in Pakistan to find out the key reasons for delayed presentation.

On the other hand, our research has several strengths. In person, one-on-one in-depth interviews in local language with a female interviewer were conducted. Anonymity was also maintained which facilitated an open and candid discussion. Additionally, we used several recommended strategies to ensure reliability, including audio taping of all twenty-four of the interviews and independent development of a coding scheme.

CONCLUSION

A significant percentage of women with breast cancer in Pakistan delay presentation primarily because of lack of awareness about the disease and its management. Along with the need to be examined by female doctors only, failure

to understand breast cancer symptoms and ignoring them are both identified as significant risk factors for delayed presentation. Cultural traditions and religious beliefs play an important role in women's Breast cancer perceptions and ultimately treatment. Understanding the benefits of early detection and presentation of Breast cancer among women was poor overall. Coordinated efforts are hence needed from the public health department regarding awareness about breast cancer and its therapeutic outcomes, to educate the women and remove the barriers identified. This study can serve as a guide for further surveys to help formulate an effective media campaign countering identified barriers in favor of mass screening programs and raising awareness among breast cancer patients to present early in clinics to help reduce the disease burden in Pakistan.

Author Affiliations: Department of surgery, Shalamar Medical & Dental College, Lahore, Pakistan

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Appendix I

Interview Guide

The patient interviews would explore at least following themes which have been previously identified in the literature. The patient's medical record would also be used to retrieve pertinent data for the research.

Category	Theme	Subtheme	Possible Questions
Delay in Presentation	Lack of Knowledge	Knowledge about Cancer	• What do you know about cancer? • What is your opinion about the cancer treatments? • Do you think cancer is a treatable condition, if so why?
		Knowledge about Breast Cancer	• What do you know about breast cancer? • How do you find about it? • What do you know about breast cancer treatment? • Is there any importance of knowing about the breast cancer early? If so what? • Is TV, Cable or social media effectively projecting this issue? Give your opinion.
		Lack of Awareness about Breast Self Examination	• Do you know any method to know about the breast cancer early? • Do you have any idea about the Breast Self Examination?
		Lack of awareness about Breast Screening	• What do you know about the breast screening? • What screening methods do you know of? • Are you aware about Pink Ribbon? • Are you aware of the annual breast cancer day?
	Working with Symptoms		• When did you first notice anything different in your breast? • What did you do about it? • Did you feel ashamed to talk somebody about it? • When did you seek any medical attention?
	Socioeconomic Issues	Cultural & Religious Issues	• What do people and friends think about breast cancer in your house? • What religion do you belong and what are the religious directions about such a disease? • How would your mother or aunt proceed if she

Delay in Diagnosis	**Lack of Resources**		• had breast cancer? • What is your attitude about it? • Did you go to some spiritual healer or herbal healer? • Did it work?
		Economic Issues	• Do you think your financial condition is linked to this delay in coming to the doctor? • Would you have been come early to the breast clinic had you been financially better?
		Educational Status	• How educated you are? • Had you been further educated, would have you sought help to the doctor early? • Do you think your education matters in terms of your attitude towards the breast cancer treatment?
		Lack of Facilities	• Do you feel our community has adequate facilities for dealing with breast cancer? Please elaborate.
		Lack of Human Resources & Expertise	• Were the doctors competent enough to diagnose your breast problem timely? • If yes how? If not why not? • Is out breast clinic staff well trained?
			• How could have your delayed diagnosis may have been prevented? Give you opinion.

Archives of Surgical Research | Original Research Communication

Appraisal Of Current Guidelines Regarding The Management Of Breast Cancer Using The Appraisal Of Guidelines Research And Evaluation (AGREE) Instrument: A Critical Review

Hadia Baig, Talat Waseem

ABSTRACT With rapid advancements in breast oncology, there is a growing need for high-quality, systematically developed clinical practice guidelines (CPGs) and consensus statements (CSs). This study aims to assess the quality of the current clinical practice guidelines and consensus statements related to the management of breast cancer employing the Appraisal of Guidelines Research and Evaluation (AGREE) II tool.

METHODS A systematic literature search of bibliographic databases (PubMed and Google Scholar) and 20 professional society websites was conducted from January 2019 onwards. Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument was used to evaluate the methodological quality of the included CPGs and CSs.

RESULTS The analysis of the AGREE II overall assessment of CPGs and CSs revealed a wide overall score range. The median overall score across the guidelines was 61%. The highest overall score was obtained by the American Society of Clinical Oncology (ASCO) guidelines, with scores ranging from 80-91%, followed by 5th ESO-ESMO ABC5 (77%), 4th ESO-ESMO BCY4 (76%) and V.4 NCCN (74%). Overall, CSs had a lower quality in the majority of the domains as compared to CPGs.

CONCLUSIONS The authors believe that the guidelines related to breast cancer management have a wide room for improvement. There is a growing need for CPGs/CSs that employ uniformly endorsed standards. Guideline development standards are the current state-of-the-art, and guideline developers must direct their efforts towards acknowledging and incorporating them into guidelines.

KEYWORDS breast cancer, management, AGREE II instrument, clinical practice guidelines, guidelines, consensus, quality of guidelines

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Critical Review

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Dr. Hadia Munir Baig, MBBS, Intern in the Department of Surgery, Shalamar Medical & Dental College, Lahore, Pakistan
hadiabaig@live.com
092 – 322 - 4567292
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As of January 2021, breast cancer has transcended lung cancer, becoming the most prevalent cancer worldwide. As stated by the World Health Organization (WHO), during the year 2020, 2.3 million women were diagnosed with Breast Cancer, resulting in 685 000 deaths globally[1]. Healthcare systems worldwide utilize evidence-based guidelines to facilitate standardized, high-quality treatment decisions and patient care. Previous evaluations have shown profound variances in the quality of breast cancer management guidelines developed by organizations across the nations [2–4]. With an overwhelming volume of scientific evidence of uncertain value, now more than ever, critically appraised clinical practice guidelines (CPGs) and consensus statements (CSs) are a fundamental component of clinical practice. When rigorously developed, they have the potential to transform complex scientific research findings into guidelines of substantial quality that can be applied to target populations globally. It is crucial to analyze the variations in the recommendations made by different organizations, as conflicting and ambiguous statements can render clinicians feeling uncertain about which treatment plan to undertake, leading to adverse patient outcomes. Prior to guideline implementation, there are certain key factors that need to be appraised, including the guideline development process involving key stakeholders, the methodological strategy used, its applicability and the clarity of presentation. The Appraisal of Guidelines for Research and Evaluation (AGREE) II Instrument is a popular, internationally validated assessment tool developed by the AGREE Collaboration, that evaluates the methodological quality of CPGs/CSs. The AGREE Collaboration define the quality of guidelines as the "confidence that the potential biases of guideline development have been addressed adequately and that the recommendations are both internally and externally valid, and are feasible for practice"[5].

In this study, we carried out a systematic review of the recent CPGs and CSs related to breast cancer management and appraised their methodological quality by employing the AGREE II instrument.

METHODS

We performed a systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[6].

Data sources and searches: An independent systematic literature search was conducted by the two authors using PubMed and Google Scholar databases applying MeSH terms, "breast cancer", "breast neoplasms", "guidelines", "practice guidelines", "consensus", "management", "therapy", "treatment" and other alternative wordings, within a 2-year window, from January 2019 till present. The main ground for searching within this 2-year window was based on Vernooij et al.'s systematic review of methodological handbooks. They stated that "handbooks recommend a time frame between publishing a CPG and commencing an updating process, with two to three years being the most frequently recommended"[7]. The exclusion of obsolete guidelines allows us to focus on updated CPGs/CSs that have incorporated new evolving researches and developments in therapy. Only full-text English Language articles were selected. A search was also carried out across 20 professional society websites and bibliographies of well-known publications. The two authors gathered to compile the available information ensuring that there were no discrepancies and that no relevant material was missed.

Inclusion and exclusion criteria: This study includes CPGs and CSs related to breast cancer management developed by national and international professional organizations and societies.

We included CPGs and CSs if the following criteria were met:

1. Concerning any or all aspects of breast cancer management including, surgical (i.e., breast surgery, axillary surgery and breast reconstruction) and systemic management (i.e., neo- and adjuvant chemotherapy, radiotherapy and endocrine treatment).
2. Related to breast cancer in men and women.
3. Related to breast cancer management in Covid-19 Pandemic
4. Including early, locally advanced and metastatic breast cancer
5. Articles in the English Language
6. Full-text available
7. Published and unpublished guidelines

Our exclusion criteria were the following:

1. CPGs/CSs related to breast cancer risk assessment, screening, diagnosis and follow-up
2. Guidelines related to prevention and treatment of symptoms and adverse events induced by breast cancer therapies
3. Substituting obsolete guidelines for updates by the same organization
4. Randomized control trials, clinical trials, narrative reviews, discussion articles, survey papers, population-based studies and case reports

Guideline quality assessment: The authors appraised the quality of the included CPGs/CSs independently using the AGREE II tool. To avoid any discrepancies in the results, the appraisers carried out a discussion to reach a consensus.

The AGREE II tool is comprised of 23 items arranged into 6 domains, each domain highlighting a unique characteristic of guideline quality. These include domain 1 (Scope and Purpose), domain 2 (Stakeholder Involvement), domain 3 (Rigor of Development), domain 4 (Clarity and Presentation), domain 5 (Applicability) and domain 6 (Editorial Independence)[5].

Appraisers scored individual items on a 7-point scale, ranging between 1 or strongly disagree and 7 or strongly agree. The domain scores were calculated by adding together the appraisers' scores for each item and scaling it as a percentage of the maximum possible score by using the formula[5]:

Domain score = (obtained score-minimum possible score)/(maximum possible score-minimum possible score)

An overall guideline assessment score was calculated by obtaining the mean score of the 6 domains. We then applied cut-off points to draw a distinction between high- and low-quality guidelines, with CPGs/CSs being 'recommended' if they had scores above 80%, 'recommended with modifications' if scores were between 50-80% and 'not recommended' if scores were below 50%[8].

RESULTS

Study selection: A total of 555 records were obtained, out of which 537 were from online databases (PubMed and Google Scholar) and 18 from additional sources (professional society websites and bibliographies from well-known publications). Of these, 50 publications were duplicates and 460 did not fulfil the selection criteria. A sum of 45 articles (37 CPGs[9–45] and 8 CSs[46–53]) were identified for the final evaluation. This information has been laid out in a tabulated form in Table 1. The study selection process has been detailed in a PRISMA flow diagram provided in Figure 1. The ICCs of the appraisers for each CPG/CS ranged between 0.9-0.96 in AGREE II.

Table 1: CPGs and CSs included

Title	Abbreviated Name	Entity	Year	Country	Published in Journal
Guidance for the management of early breast cancer Recommendations and practice points	Australia Early BC	AG	2020	Australia	Not Published
AGO Recommendations for the Diagnosis and Treatment of Patients with Locally Advanced and Metastatic Breast Cancer: Update 2019	AGO LABC/MBC 2019	AGO	2020	Germany	Breast Care
AGO Recommendations for the Diagnosis and Treatment of Patients with Early Breast Cancer: Update 2021	AGO Early BC 2021	AGO	2021	Germany	Breast Care
Systemic Therapy for Early Breast Cancer	AHS systemic for Early BC	AHS	2021	Canada	Not Published
Consensus Guideline on the Management of the Axilla in Patients With Invasive/In-Situ Breast Cancer	ASBrS Axilla Invasive BC	ASBrS	2019	USA	Not Published
Endocrine Treatment and Targeted Therapy for Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer: ASCO Guideline Update	ASCO Endocrine & Targeted therapy for HR+/HER2-MBC	ASCO	2021	USA	JCO
Chemotherapy and Targeted Therapy for Patients With Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer That is Either Endocrine-Pretreated or Hormone Receptor–Negative: ASCO Guideline Update	ASCO Chemo- & Targeted therapy for HER2- MBC	ASCO	2021	USA	JCO
Selection of Optimal Adjuvant Chemotherapy and Targeted Therapy for Early Breast Cancer: ASCO Guideline Update	ASCO Chemo- & Targeted Therapy for Early BC	ASCO	2020	USA	JCO
Management of the Axilla in Early-Stage Breast Cancer: Ontario Health (Cancer Care Ontario) and ASCO Guideline	ASCO Axilla Early BC	ASCO	2021	USA	JCO
Management of Male Breast Cancer: ASCO Guideline	ASCO Male BC	ASCO	2020	USA	JCO
Adjuvant PARP Inhibitors in Patients With High-Risk Early-Stage HER2-Negative Breast Cancer and Germline BRCA Mutations: ASCO Hereditary Breast Cancer Guideline Rapid Recommendation Update	ASCO Hereditary BC	ASCO	2021	USA	JCO
Use of Endocrine Therapy for Breast Cancer Risk Reduction: ASCO Clinical Practice Guideline Update	ASCO BC Risk Reduction	ASCO	2019	USA	JCO
Neoadjuvant Chemotherapy, Endocrine Therapy, and Targeted Therapy for Breast Cancer: ASCO Guideline	ASCO Chemo-, Endo- & Targeted Therapy for BC	ASCO	2021	USA	JCO
Breast cancer management guidelines during COVID-19 pandemic	India Covid-19 BC	ASI	2020	India	IJS
Chinese Expert Consensus on the Clinical Diagnosis and Treatment of Advanced Breast Cancer (2018)	China Advanced BC	CACA	2020	China	ACS Journals
Clinical practice guidelines for modified radical mastectomy of breast cancer: Chinese Society of Breast Surgery (CSBrs) practice guidelines 2021	China MRM BC 2021	CSBrs	2021	China	CMJ
Clinical practice guidelines for diagnosis and treatment of invasive breast cancer: Chinese Society of Breast Surgery (CSBrS) practice guidelines 2021	China Invasive BC 2021	CSBrs	2021	China	CMJ
Clinical practice guidelines for breast cancer implantable intravenous infusion ports: Chinese Society of Breast Surgery practice guidelines 2021	China BC implantable ports	CSBrs	2021	China	CMJ
Clinical practice guideline for breast-conserving surgery in patients with early-stage breast cancer: Chinese Society of Breast Surgery (CSBrS) practice guidelines 2021	China BCS Early BC 2021	CSBrs	2021	China	CMJ
5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5)	5th ESO-ESMO ABC5	ESO, ESMO	2020	Europe	Annals Of Oncology
ESO-ESMO 4th International Consensus Guidelines for Breast Cancer in Young Women (BCY4)	4th ESO-ESMO BCY4	ESO, ESMO, EUSOMA	2020	Europe	Annals Of Oncology
Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up	ESMO Early BC	ESMO	2019	Europe	Annals Of Oncology
GEICAM Guidelines for the Management of Patients with Breast Cancer During Spain's COVID-19 Pandemic	GEICAM BC Covid-19	GEICAM	2020	Spain	The Oncologist

International multidisciplinary expert panel consensus on breast reconstruction and radiotherapy	IMEP BR & RT	IMEP	2019	Europe	BJS
The Japanese Breast Cancer Society clinical practice guidelines for surgical treatment of breast cancer	Japanese surgical BC	JBCS	2019	Japan	Breast Cancer
The Japanese Breast Cancer Society Clinical Practice Guidelines, 2018 edition: the tool for shared decision making between doctor and patient	Japanese SDM BC	JBCS	2019	Japan	Breast Cancer
The Japanese breast cancer society clinical practice guidelines for systemic treatment of breast cancer	Japanese systemic BC	JBCS	2020	Japan	Breast Cancer
Breast cancer management during the COVID 19 pandemic: French guidelines	France Covid-19 BC	Multiple groups	2020	France	Eur J Breast Health
NCA Breast Cancer Clinical Guidelines	NCA BC	NCA	2020	UK	Not Published
Breast cancer, version 4.2021 featured updates to the NCCN guidelines	V.4 NCCN	NCCN	2021	USA	JNCCN
Chinese guidelines for diagnosis and treatment of breast cancer 2018 (English version)	China BC diagnosis & treatment	NHCPRC	2019	China	CJCRCN
Trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after 2 or more anti-HER2 therapies	NICE Trastuzumab deruxtecan	NICE	2021	UK	Not Published
Ribociclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy	NICE Ribociclib & Fulvestrant	NICE	2021	UK	Not Published
Atezolizumab with nab-paclitaxel for untreated PD-L1-positive, locally advanced or metastatic, triple-negative breast cancer	NICE Atezolizumab & Nab-paclitaxel	NICE	2020	UK	Not Published
Trastuzumab emtansine for adjuvant treatment of HER2-positive early breast cancer	NICE trastuzumab emtansine	NICE	2020	UK	Not Published
Palbociclib with fulvestrant for treating hormone receptor-positive, HER2-negative, advanced breast cancer	NICE Palbociclib & Fulvestrant	NICE	2020	UK	Not Published
Neratinib for extended adjuvant treatment of hormone receptor-positive, HER2-positive early stage breast cancer after adjuvant trastuzumab	NICE Neratinib	NICE	2019	UK	Not Published
Abemaciclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy	NICE Abemaciclib & Fulvestrant	NICE	2019	UK	Not Published
Pertuzumab for adjuvant treatment of HER2-positive early stage breast cancer	NICE Pertuzumab	NICE	2019	UK	Not Published
Abemaciclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer	NICE Abemaciclib & Aromatase Inhibitor	NICE	2019	UK	Not Published
SEOM clinical guidelines in advanced and recurrent breast cancer (2018)	SEOM Advanced & Recurrent BC	SEOM	2019	Spain	CTO
Customizing Local and systemic therapies for women with early breast cancer: The St. Gallen International Consensus Guidelines for treatment of early breast cancer 2021	St. Gallen 2021	St. Gallen	2021	Europe	Annals Of Oncology
Guidelines on Management of the Patient with Breast Cancer	BC	UWI, UHWI, ASJ	2019	West Indies/ Jamaica	West Indian Med J
Evidence-based guidelines for managing patients with primary ER+ HER2− breast cancer deferred from surgery due to the COVID-19 pandemic	Primary ER+ deferred BC	---	2020	International	NPJ Breast Cancer
2020 consensus guideline for optimal approach to the diagnosis and treatment of HER2-positive breast cancer in Bosnia and Herzegovina	BiH HER2+ BC	---	2020	BiH	BJBMS

Table 1. ABBREVIATIONS: American Cancer Society, ACS; Arbeitsgemeinschaft Gynakologische Onkologie, AGO; Alberta Health Services, AHS; American Society of Breast Surgeons, ASBrS; American Society of Clinical Oncology, ASCO; Association of Surgeons of India, ASI; Association of Surgeons in Jamaica, ASJ; Australian Government, AG; Bosnia and Herzegovina, BiH; Breast Cancer, BC; Bosnian Journal of Basic Medical Sciences, BJBMS; British Journal of Surgery, BJS; Chinese Anti-Cancer Association, CACA; Chinese Society of Breast Surgery, CSBrs; Chinese Journal of Cancer Research, CJCRCN; CPG, Clinical practice guideline; Clinical and Translational Oncology, CTO; Consensus statement, CS; European School of Oncology, ESO; European Society for Medical Oncology, ESMO; European Society of Breast Cancer Specialists, EUSOMA; Indian Journal of Surgery, IJS; International multidisciplinary expert panel, IMEP; Journal of Clinical Oncology, JCO; Journal of the National Comprehensive Cancer Network, JNCCN; Breast Expert Advisory Group/ Northern Cancer Alliance, NCA; National Comprehensive Cancer Network, NCCN; National Health Commission of the People's Republic of China, NHCPRC; National Institute for Health and Care Excellent, NICE; Nature Portfolio journals, NPJ; Sociedad Espanola de Oncología Medica, SEOM; University of the West Indies, UWI; University Hospital of the West Indies, UHWI

Figure 1: PRISMA Flow Diagram of the Search Strategy
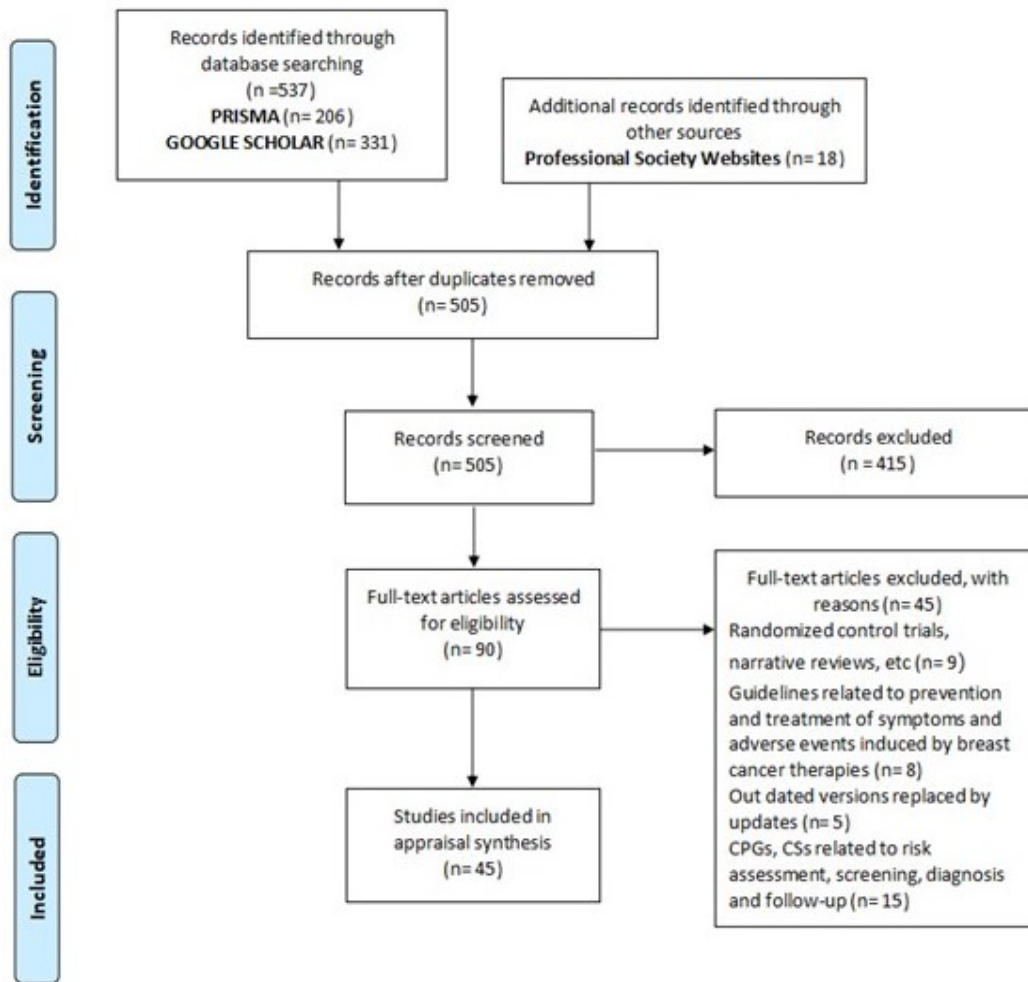
Fig. 1. The study selection process has been detailed in a PRISMA flow diagram.

GUIDELINES APPRAISAL

Overall Quality Assessment: The analysis of the AGREE II overall assessment of CPGs and CSs revealed scores over a wide spectrum (Figure 2). The median overall score across the guidelines was 61%. The highest overall score was obtained by the American Society of Clinical Oncology (ASCO)[13–20] guidelines, with scores ranging from 80-91%, followed by [5th] ESO-ESMO ABC5[48] (77%), [4th] ESO-ESMO BCY4[50] (76%) and V.4 NCCN[34] (74%). The lowest scores were obtained by French[28] guidelines (16%) and guidelines by NHCPRC[32] (17%). Only 8 out of 45 (18%) of CPGs/CSs were in the 'recommended' zone, 25 (56%) were in the 'recommended with modifications' zone and 12 (27%) were in the 'not recommended' zone.

Domain Assessment: There was a profound disparity in the quality across the domains (Figures 3a-f). Across the guidelines, we observed the highest mean score in Domain 1 (Scope and Purpose) (83.7%), followed by Domain 6 (Editorial Independence) (75.4%) and Domain 4 (Clarity and Presentation) (68.3%). The lowest mean scores were observed in Domain 5 (Applicability) (40.2%) and Domain 2 (Stakeholder Involvement) (49.1%). Figures 3a-f depict the assessments at a domain level.

CPGs vs. Consensus Statements: This study included 37 CPGs and 8 CSs. Overall, CSs had a lower quality in the majority of the domains as compared to CPGs. The median (range) in 'Scope and Purpose' was CPG 88% vs. CSs 85.5%, 'Stakeholder Involvement' CPG 54% vs. CSs 31.5%, 'Rigor of Development' CPG 53% vs. CSs 38% and 'Applicability' CPG 43% vs. CSs 41.5%.

The ASCO13–20 CPGs (80-91%) had the highest quality, whereas 5th ESO-ESMO ABC548 (77%) and 4th ESO-ESMO BCY450 (76%) had the highest quality in the CSs.

DISCUSSION

Main Findings: Our study demonstrated that the median overall quality (61%) of the guidelines was somewhat improved compared to M Maes-Carballo et al.'s[4] previous study (54%). 8 out of 45 guidelines were above 80%, in the 'recommended' zone and were considered of high-quality. It was found that ASCO[13–20], ESO-ESMO[26,48,50], and NCCN[34] CPGs/CSs had the highest scoring overall assessments, whereas France[27], NHCPRC[32] and ASBrS[46] had the lowest. Our evaluation showed that CPGs had a better overall quality as compared to CSs.

We are aware that several factors are involved during the development of CPGs/CSs, including differing perspectives, conditions, available resources, and time-frames available to the organizations among others. The values and views of guideline developers and how they weigh evidence is reflected in their recommendations. Furthermore, we must therefore also consider that breast cancer management guidelines related to the Covid-19 pandemic were developed during these uncertain conditions with perhaps shorter time-frames involved.

Limitations: We included only full-text English Language articles within a 2-year window from January 2019 onwards.

Therefore, we understand that several commendable guidelines by credible organizations would have been excluded. The guidelines included had differing themes. We did not distinctively weigh individual domains' relative importance, although some have a more pivotal role in generating practical, high-quality guidelines than others. The appraisal was based on each item's given information, but the inability to quantify this provided information made it a subjective process.

CONCLUSION

The authors believe that the guidelines related to breast cancer management have a wide room for improvement. There is a growing need for CPGs/CSs that employ uniformly endorsed standards. Guideline development standards are the current state-of-the-art, and guideline developers must direct their efforts towards acknowledging and incorporating them into guidelines. High-quality evidence and a standardized guideline development process are prerequisites for trustworthy, resource-stratified CPGs/CSs utilized in individual patient encounters.

Figure 2.

AGREE II Overall Assessment Scores Of CPGs & CSs

Figure 3a.

Domain 1 (Scope and Purpose)

Guideline	%
V.4 NCCN	100%
5th ESO-ESMO ABC5	100%
4th ESO-ESMO BCY4	100%
St. Gallen 2021	97%
SEOM Advanced & Recurrent BC	97%
NICE Trastuzumab deruxtecan	97%
NICE Ribociclib & Fulvestrant	97%
Japanese SDM BC	97%
China Advanced BC	97%
BiH HER2+ BC	97%
NICE trastuzumab emtansine	94%
NICE Pertuzumab	94%
NICE Palbociclib & Fulvestrant	94%
NICE Neratinib	94%
NICE Atezolizumab & Nab-paclitaxel	94%
NICE Abemaciclib & Fulvestrant	94%
NICE Abemaciclib & Aromatase Inhibitor	94%
ASCO Male BC	94%
ASCO Endocrine & Targeted therapy for HR+/HER2- MBC	94%
ASCO Axilla Early BC	94%
Japanese systemic BC	91%
ASCO Chemo- & Targeted therapy for HER2- MBC	91%
ASCO Chemo-, Endo- & Targeted Therapy for BC	88%
ASCO Chemo- & Targeted Therapy for Early BC	88%
ASCO BC Risk Reduction	88%
AGO Early BC 2021	88%
Japanese surgical BC	86%
IMEP BR & RT	86%
GEICAM BC Covid-19	86%
Primary ER+ deferred BC	83%
ASBrS Axilla Invasive BC	80%
ESMO Early BC	77%
AGO LABC/MBC 2021	77%
France Covid-19 BC	75%
Australia Early BC	75%
ASCO Hereditary BC	75%
India Covid-19 BC	72%
BC	72%
China BC diagnosis & treatment	69%
China MRM BC 2021	66%
China Invasive BC 2021	66%
China BCS Early BC 2021	66%
China BC implantable ports	66%
NCA BC	30%
AHS systemic for Early BC	22%

Figure 3b.

Domain 2 (Stakeholder Involvement)

Guideline	%
ASCO Axilla Early BC	94%
NICE Trastuzumab deruxtecan	86%
NICE Ribociclib & Fulvestrant	86%
ASCO Chemo- & Targeted therapy for HER2- MBC	80%
ASCO BC Risk Reduction	80%
St. Gallen 2021	75%
ASCO Endocrine & Targeted therapy for HR+/HER2- MBC	75%
Australia Early BC	72%
Japanese SDM BC	69%
ASCO Chemo-, Endo- & Targeted Therapy for BC	69%
ASCO Chemo- & Targeted Therapy for Early BC	69%
China MRM BC 2021	66%
China Invasive BC 2021	66%
China BCS Early BC 2021	66%
China BC implantable ports	66%
AHS systemic for Early BC	66%
ASCO Male BC	63%
NICE trastuzumab emtansine	55%
NICE Pertuzumab	55%
NICE Palbociclib & Fulvestrant	55%
NICE Neratinib	55%
NICE Atezolizumab & Nab-paclitaxel	55%
NICE Abemaciclib & Fulvestrant	55%
NICE Abemaciclib & Aromatase Inhibitor	55%
Japanese surgical BC	52%
BiH HER2+ BC	50%
GEICAM BC Covid-19	44%
AGO LABC/MBC 2021	44%
AGO Early BC 2021	44%
China Advanced BC	38%
India Covid-19 BC	36%
ASCO Hereditary BC	36%
SEOM Advanced & Recurrent BC	33%
BC	33%
Japanese systemic BC	30%
ASBrS Axilla Invasive BC	30%
5th ESO-ESMO ABC5	28%
4th ESO-ESMO BCY4	28%
ESMO Early BC	27%
V.4 NCCN	25%
IMEP BR & RT	25%
Primary ER+ deferred BC	19%
France Covid-19 BC	16%
NCA BC	5%
China BC diagnosis & treatment	3%

Figure 3c.

Domain 3 (Rigour of Development)

Guideline	%
AHS systemic for Early BC	96%
ASCO Hereditary BC	93%
ASCO BC Risk Reduction	92%
ASCO Chemo- & Targeted therapy for HER2- MBC	90%
ASCO Chemo- & Targeted Therapy for Early BC	90%
ASCO Endocrine & Targeted therapy for HR+/HER2- MBC	88%
ASCO Axilla Early BC	88%
ASCO Chemo-, Endo- & Targeted Therapy for BC	84%
V.4 NCCN	82%
ASCO Male BC	77%
5th ESO-ESMO ABC5	76%
4th ESO-ESMO BCY4	73%
NICE Trastuzumab deruxtecan	71%
NICE Ribociclib & Fulvestrant	71%
Japanese systemic BC	70%
Japanese SDM BC	65%
Australia Early BC	63%
IMEP BR & RT	62%
Japanese surgical BC	56%
AGO Early BC 2021	55%
AGO LABC/MBC 2021	54%
NICE trastuzumab emtansine	53%
NICE Pertuzumab	53%
NICE Palbociclib & Fulvestrant	53%
NICE Neratinib	53%
NICE Atezolizumab & Nab-paclitaxel	53%
NICE Abemaciclib & Fulvestrant	53%
NICE Abemaciclib & Aromatase Inhibitor	53%
ESMO Early BC	51%
China Advanced BC	40%
SEOM Advanced & Recurrent BC	36%
China Invasive BC 2021	27%
China MRM BC 2021	26%
China BCS Early BC 2021	26%
China BC implantable ports	26%
St. Gallen 2021	24%
NCA BC	21%
BiH HER2+ BC	17%
ASBrS Axilla Invasive BC	15%
GEICAM BC Covid-19	14%
BC	13%
Primary ER+ deferred BC	10%
India Covid-19 BC	6%
France Covid-19 BC	1%
China BC diagnosis & treatment	1%

Figure 3d.

Domain 4 (Clarity and Presentation)

Guideline	%
ASCO Hereditary BC	100%
ASCO BC Risk Reduction	100%
5th ESO-ESMO ABC5	100%
4th ESO-ESMO BCY4	100%
V.4 NCCN	97%
Japanese systemic BC	97%
AGO LABC/MBC 2021	97%
AGO Early BC 2021	97%
ASCO Male BC	94%
ASCO Chemo-, Endo- & Targeted Therapy for BC	94%
ASCO Chemo- & Targeted Therapy for Early BC	94%
ASCO Axilla Early BC	94%
ASCO Endocrine & Targeted therapy for HR+/HER2- MBC	91%
ASCO Chemo- & Targeted therapy for HER2- MBC	88%
ESMO Early BC	86%
GEICAM BC Covid-19	83%
AHS systemic for Early BC	83%
SEOM Advanced & Recurrent BC	77%
NCA BC	77%
China Advanced BC	77%
BiH HER2+ BC	77%
Australia Early BC	72%
NICE trastuzumab emtansine	69%
NICE Pertuzumab	69%
NICE Palbociclib & Fulvestrant	69%
NICE Neratinib	69%
NICE Atezolizumab & Nab-paclitaxel	69%
NICE Abemaciclib & Fulvestrant	69%
NICE Abemaciclib & Aromatase Inhibitor	69%
BC	63%
China Invasive BC 2021	61%
Japanese surgical BC	58%
China MRM BC 2021	58%
China BCS Early BC 2021	58%
China BC implantable ports	58%
Japanese SDM BC	55%
NICE Trastuzumab deruxtecan	52%
NICE Ribociclib & Fulvestrant	52%
St. Gallen 2021	42%
IMEP BR & RT	38%
India Covid-19 BC	27%
ASBrS Axilla Invasive BC	27%
Primary ER+ deferred BC	13%
China BC diagnosis & treatment	8%
France Covid-19 BC	5%

Figure 3e.

Domain 5 (Applicability)

Guideline	Applicability
ASCO Chemo-, Endo- & Targeted Therapy for BC	95%
ASCO Male BC	91%
ASCO Chemo- & Targeted therapy for HER2- MBC	83%
China Advanced BC	81%
ASCO Axilla Early BC	77%
GEICAM BC Covid-19	72%
ASCO Hereditary BC	69%
ASCO Chemo- & Targeted Therapy for Early BC	62%
5th ESO-ESMO ABC5	60%
4th ESO-ESMO BCY4	56%
ASCO Endocrine & Targeted therapy for HR+/HER2- MBC	52%
V.4 NCCN	50%
BiH HER2+ BC	50%
ASCO BC Risk Reduction	50%
NCA BC	47%
ESMO Early BC	47%
NICE Trastuzumab deruxtecan	45%
NICE Ribociclib & Fulvestrant	45%
Australia Early BC	45%
AGO Early BC 2021	45%
NICE trastuzumab emtansine	43%
NICE Pertuzumab	43%
NICE Palbociclib & Fulvestrant	43%
NICE Neratinib	43%
NICE Atezolizumab & Nab-paclitaxel	43%
NICE Abemaciclib & Fulvestrant	43%
NICE Abemaciclib & Aromatase Inhibitor	43%
AGO LABC/MBC 2021	41%
BC	39%
St. Gallen 2021	33%
Japanese systemic BC	33%
India Covid-19 BC	31%
AHS systemic for Early BC	29%
Primary ER+ deferred BC	22%
China BC diagnosis & treatment	22%
Japanese SDM BC	18%
IMEP BR & RT	10%
China MRM BC 2021	10%
China Invasive BC 2021	10%
China BCS Early BC 2021	10%
China BC implantable ports	10%
SEOM Advanced & Recurrent BC	6%
Japanese surgical BC	2%
France Covid-19 BC	0%
ASBrS Axilla Invasive BC	0%

Figure 3f.

Domain 6 (Editorial Independence)

Guideline	Editorial Independence
V.4 NCCN	100%
St. Gallen 2021	100%
SEOM Advanced & Recurrent BC	100%
NICE trastuzumab emtansine	100%
NICE Trastuzumab deruxtecan	100%
NICE Ribociclib & Fulvestrant	100%
NICE Pertuzumab	100%
NICE Palbociclib & Fulvestrant	100%
NICE Neratinib	100%
NICE Atezolizumab & Nab-paclitaxel	100%
NICE Abemaciclib & Fulvestrant	100%
NICE Abemaciclib & Aromatase Inhibitor	100%
Japanese surgical BC	100%
ASCO Male BC	100%
ASCO Hereditary BC	100%
ASCO Endocrine & Targeted therapy for HR+/HER2- MBC	100%
ASCO Chemo-, Endo- & Targeted Therapy for BC	100%
ASCO Chemo- & Targeted therapy for HER2- MBC	100%
ASCO Chemo- & Targeted Therapy for Early BC	100%
ASCO BC Risk Reduction	100%
ASCO Axilla Early BC	100%
AHS systemic for Early BC	100%
AGO Early BC 2021	100%
5th ESO-ESMO ABC5	100%
4th ESO-ESMO BCY4	100%
ESMO Early BC	95%
Australia Early BC	83%
Primary ER+ deferred BC	50%
Japanese systemic BC	50%
Japanese SDM BC	50%
India Covid-19 BC	50%
IMEP BR & RT	50%
China MRM BC 2021	50%
China Invasive BC 2021	50%
China BCS Early BC 2021	50%
China BC implantable ports	50%
China Advanced BC	50%
BiH HER2+ BC	50%
AGO LABC/MBC 2021	50%
NCA BC	20%
GEICAM BC Covid-19	20%
France Covid-19 BC	10%
China BC diagnosis & treatment	10%
BC	10%
ASBrS Axilla Invasive BC	4%

Figure 3 clearly depicts the assessment at domain level.

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Archives of Surgical Research | Systematic Literature Review

The WHO Surgical Safety Checklist: A Systematic Literature Review

Sheikh Muhammad Rehman Zia, Rosheen Zahid, Hira Ashraf

IMPORTANCE In clinical settings, surgical complications are seen to be responsible for a significant proportion of morbidity and mortality each year. Surgical procedures have become mandatory for fixing uprising complex pathological complications. Advanced technologies are helpful in the diagnoses and treatment of complicated pathological cases but human errors during surgeries cannot be minimized with such technologies. To address such issues WHO has bestowed a checklist at the global level to minimize the possible surgical complications.

MATERIAL AND METHODS: This article is written according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Secondary data was selected by three steps; identification of 350 articles, thematic analysis of 38 articles, and selection of 7 articles following detailed review. The article selection process was done according to inclusion and exclusion criteria.

RESULTS A detailed review of available data shows a direct relationship between the use of surgical safety checklists and the reduction of surgical complications. Surgical risk factors in the pre-operative, operative, and post-operative phases are minimized following the implementation of the checklist. Implementation of this practice has significantly reduced human errors, thereby, improving surgical outcomes.

CONCLUSIONS Available data points towards improved surgical outcomes following the use of a surgical safety checklist. However, further study is required in this area to determine the exact efficacy of this practice.

KEYWORDS WHO Checklist, Surgical Complications, Surgical Settings, Surgical Procedures, Health Outcomes

pproximately 234 million operations are performed annually in 192 member states of WHO[1]. With the uprising incidence of trauma, congenital anomalies acquired diseases, and cancers surgical care has become the indispensable component of the public health care system[2]. Surgical complications can be real harm to the patients. To increase the accuracy and efficiency of surgical procedures, surgical teams must perform error-proof and safe procedures. Hence, in a modern healthcare system, surgical safety has become a vital component.

In 2008 WHO introduced the implementation of a surgical safety checklist to improve outcomes of surgical interventions. It was proposed to identify human errors and possible surgical complications that compromise the safety and outcomes of surgical interventions[2]. The surgical safety checklist addressed the issues of scrutiny, the efficiency of the procedure, and patient outcome in pre-operative, operative, and post-operative phases. In addition, it addressed the issues faced by patients during their stay in recovery and ward. The mandatory checkpoints are before induction of anesthesia, surgical incision, and patient leaving the operation room[3].

Advancements in anesthesiology, super-specialties in surgical practice, and safe perioperative intensive care have made complicated procedures safe and viable. However, it is important to highlight that advancement in surgical procedures doesn't ensure safe practice. Human errors are attributed to negligence, incorrect attitudes, and overconfidence. Moreover, functioning which has no practical shreds of evidence leads towards complications. So the introduction of a safety checklist in general practice that is recognized beneficial by international health care institutes should be implemented in operation theatres to make the procedures safer [4].

Existing data have supported the idea that the most common errors in operating rooms are communication errors which resulted in a reduction of operational accuracy. Coordination and cooperation between surgical team members are essential components for better service delivery. Miscommunication or lack of communication can affect patient safety and is a major factor to cause adverse incidents. In a complex environment of operating rooms, an effective exchange of information is required between team members for incident prevention and incident recovery.

Without effective communication, the interdependent goal of effective and safe surgical intervention is not coordinated. Surgical cases are seen to be affected due to these failures in 90% of cases. Implementation and execution of the surgical safety checklist accurately may reduce the complications and communication errors leading to a reduction in morbidity and mortality. Surgical safety checklist may not necessarily prevent all the possible adverse outcomes but it would provide a safer direction to the team members [4].

METHODS

The secondary data was utilized to conduct the research. The search engines which were utilized to obtain the scientific data were; Medline/PubMed, Biomed Central, NIH, open MD, and Web Med. After recruitment, the data was selected based on the inclusion criteria. To further refine the data, qualitative analyses and metanalyses were performed. Specific keywords were used on the search engine to obtain only related articles.
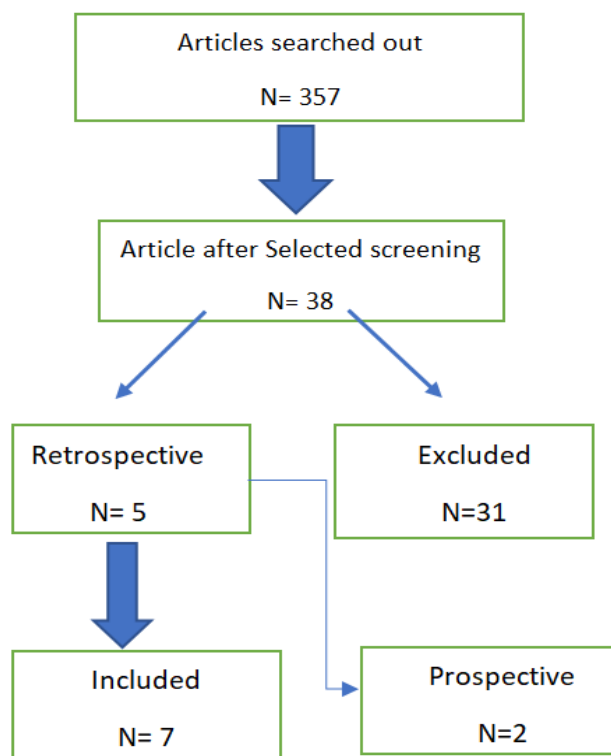
Inclusion Criteria: The guidelines of PRISMA were used for the inclusion of the data in the systematic review. To include the data, the procedure was divided into three steps; identification, primary selection, and final selection. In the first step, 357 articles were identified. Out of 357, 38 articles were selected in the second step. For the systematic scientific review, 7 most relevant and admissible articles were selected for the final studies. The selected articles were

peer-reviewed, based on the randomized trials, containing clear abstracts, and were no older than ten years.

Exclusion Criteria: The articles older than ten years, without any abstract and background information were excluded. Articles with fewer references and with a lack of proper author information and affiliation were rejected. Moreover, the articles published in unrecognized journals were also not included.

Data Extraction and Metanalyses: The selected journals and articles were further processed for the data extraction. The only required data was extracted which was organized in a specific tabular form. Physical coding was utilized to locate the data. To make the data more reliable it was cross-checked by three reviewers. Meta-analyses were performed to check the strength of presented pieces of evidence in the selected journals and articles.

RESULTS:

The findings obtained from the selected studies were promising in favor of the implementation of a checklist in surgical settings intending to reduce surgical complications. A Variety of consequences including barriers to implementation, adverse events, and facilitators were included to analyze the results. It has been observed that the checklist provided a positive role in the safety of perioperative care and the safety of the patient in a wide range of surgical settings. The World Health Organization recommended checklists were associated with significant reduction of surgical complications, detection of safety hazards, and improvement in the communication among operating staff members. Designed strategies for the execution of the checklists included incorporating staff feedback and enlisting the institutional leaders correlated with the local champions.

Most of the existing data ensured the improvement of patient safety after the implementation of the checklist. Communication strategies along with team training based on checklists are significantly associated with a reduction in surgical morbidity and mortality. Moreover, Checklists have a significant positive role in the improvement of critical surgical and health care processes, especially at surgical sites. The checklists have reduced the errors in many different ways; enhancing the communication, encouragement of non-hierarchal team approach, catching all the near misses, managing the unanticipated and anticipated complications by using technology, and through anticipation of potential complications.

DISCUSSION

Under the recommendations of the WHO, the checklist was widely implemented in a variety of contexts. The efficiency and the performance of the paper tick boxes, posters, and

electronic medical reports are still under consideration. The overall feedback from different surgical teams was positive but the feedback from anesthesiologists and nurses was more supportive than the feedback from surgeons. There are multiple reasons which have been identified for the positive outcomes of WHO checklists which are; staff understanding and good training, evenly distribution of responsibility among the team members, feeling of ownership by each team member, enhancement of the teamwork and communication, incorporation of real-time feedback, and stepwise implementation of the process[4].

Year	Author	Country	Research Method	Theme Identified
2018	Thomas G Weiser	USA	Demographic information to calculate the total worldwide volume of surgery.	234.2 (95% CI 187.2-281.2) million major surgical procedures are undertaken every year worldwide
2012	Jonathan R Treadwell	USA	A search of four databases (MEDLINE, CINAHL, EMBASE, and the Cochrane Database of Controlled Trials) was conducted f	Surgical checklists represent a relatively simple and promising strategy for addressing surgical patient safety worldwide
2015	Anne E. Pugel	USA		The surgical community should view the checklist as a tool for improving communication and safety
2015	Gordon Hale	UK	Data collected from the first two cycles were circulated to the ward staff and the initial findings from the report were discussed	Following the introduction of a structured clinical review sheet, the overall compliance with the documentation of seven outcome measures improved from 45% to 89%
2012	Shauna M Levy	USA	A prospective study was performed to evaluate the completion of all preincision components of the surgical checklist.	A total of 142 pediatric surgical cases were observed. Hospital-reported data demonstrated 100% compliance with the preincision phase of the checklist for these cases.
2014	Susan J Collins		A narrative review of the literature to determine the effectiveness of the surgical safety checklist in correcting and preventing errors in the OR	Analysis of results indicated the effectiveness of the surgical checklist in reducing the incidence of wrong-site surgeries and other medical errors;

Health Outcomes: Concerning the health outcomes, more than half of the implemented studies reported relevant results. In these relevant studies, the reductions of surgical complications were impressive. For instance, the occurrence of surgical complications was reduced from 22.9% to the level of 10%. Besides the surgical complications, the infections at the surgical sites were also reduced at a significant rate after the application of Surgical checklists. Moreover, studies of Royal Bolton revealed that about nine potential incidents were avoided just in one month of implementation of the checklist. Haynes et al performed a large multicenter prospective comparative study across 8 major cities in the world (Toronto; New Delhi; Amman; Auckland; Manila; Ifakara; London and Seattle), comparing 30-day outcomes in patients managed without a checklist (n= 3733) to those with checklist implementation (n=3955). In this study, the death rate was found to have declined from 1.5% to 0.8% (P=0.003), and inpatient complications reduced from 11.0% to 7.0% (P<0.001) in favor of WHOSSC use[5].

Possible Harms: Since WHO presented the checklist the direct harm in the surgical settings has not appeared. Both anesthesiologists and surgeons felt it caused a detrimental delay, particularly during time-critical stages of emergency procedures[6].

According to Sewell, the infection rate of lower respiratory tract infection increased from 2.1% to 2.5% after the implementation of the WHO checklist. But the real cause of this increase is still unclear and it is just an assumption without any solid proof. Despite no such reported potential harm, there is concern over potential harm by some checklist users [7]. For instance, some users are worried that about the patient anxiety after the use of the checklist. The studies of Kearns which were conducted in 2011, disclosed that more than 30% of users believed that such checklists created inconvenience, especially during emergencies. But it is important to mention that the percentage was lower when compared to prior studies (53%) conducted to find out the concern over the implementation of the checklist. There are concerns over its efficiency after the overlapping of checklist safety procedure on already practiced procedure [8].

CONCLUSION:
WHO surgical checklist is a simple and favorable strategy to address surgical patient safety worldwide. Most of the studies concluded that there are positive clinical outcomes of using the checklist. There is the utmost need for studies to evaluate the efficiency and the extent of the degree to which the checklist can improve surgical/clinical outcomes.

Author Affiliations: Shalamar Medical & Dental College, Lahore, Pakistan

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Archives of Surgical Research | Critical Review

Evolving Management Options for Breast Cancer in Era of Oncoplastic and Reconstructive Breast Surgery: Where Do We Stand?

Abubaker Shafiq Ahmed; Safia Zahir Ahmed; Noman Zaib

IMPORTANCE Recent advances in oncoplastic techniques have revolutionized concepts in the management of breast cancer. Numerous oncoplastic and reconstructive surgery options are available to oncoplastic breast surgeons to meet the needs of variation in character and stage of the disease. To employ these available surgical and non-surgical strategies, a holistic and comprehensive understanding of the disease and treatment modalities is pivotal. In this essay, we would describe various surgical options available and would critically evaluate them in light of a typical case scenario.

KEYWORDS Oncoplastic Breast Surgery; Breast Reconstruction; Implant-Based Reconstruction

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Critical Review

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author:
Abu Baker Shafiq Ahmad
Shalamar Medical & Dental College, Lahore
(abubaker_shafiq@yahoo.com)
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B reast reconstruction has become an integral part of breast cancer treatment[1]. Both autologous and implant-based reconstructions are effective but need to be individualized to the needs of patients. Annually, more than 80, 000 reconstructions in the US are implant-based, however, the utility and satisfaction of the implant-based reconstruction are gradually reducing owing to multiple reasons[2,3]. Capsular contracture, infection, the feeling of being unnatural, and finally breast implant-associated (BIA) lymphoma are the few reasons for reducing the popularity of implant-based reconstructions and the gradual shift to autologous reconstruction[4].

IMPLANT-BASED RECONSTRUCTION

Implant-based reconstructions are the most commonly performed breast reconstructions all over the world [5,6]. Nipple-sparing and skin-sparing mastectomies associated with implants are being increasingly performed and are associated with up to 7% recurrence rate over a period of 10 years, which is comparable with cancer risk in contralateral normal breast [7,8]. Implant-based reconstructions are quite suitable for small and medium-sized breasts where ptosis is limited. Round and anatomical implants with or without surface texturing are available and are associated with good aesthetic outcomes [7]. Immediate reconstructions are well suited with implant-based reconstructions. Small inframammary or lateral incisions are used for mastectomy and insertion of implants. The implants are mostly placed in a subpectoral plane with or without the use of acellular

CASE SCENARIO

A 46-year-old woman underwent previous WLE for a 15mm triple-negative Grade-3 breast cancer 1 year ago. Her surveillance mammography has shown a local recurrence, confirmed on core biopsy. She has just moved to the local area and is a single working mother to three daughters aged 6-17. She is a non-smoker and exercises regularly. Her previous medical history includes Laparoscopic cholecystectomy and emergency C-section. She is keen to undergo immediate breast reconstruction. Although she has some concerns about implants as she is aware of some risks following recent news reports but is open to any suitable option available. Please provide a comprehensive management plan for this case including a discussion on the following issues: Further investigations, management options for breast and axilla, appropriate clinical trials, reconstructive options including limitations, social and lifestyle factors, consent process, adjuvant therapy, surveillance, and follow-up, PROMS, medico-legal issues. Your plan should reference and critique relevant evidence and guidelines, and you are encouraged to cite relevant examples from your clinical practice to support your response.

dermal matrix (ADM) depending upon the availability of the coverage [9].

Implant-based reconstructions can be done either in an immediate setting or it may be bridged by using expandable Becker's prosthesis. The patients who require adjuvant chemoradiation are best treated in two stages involving

Becker's prosthesis. This, however, leads to poor aesthetic outcomes [3].

Advantages of the implant-based reconstructions include operative ease; shorter postoperative hospital stay and fewer ischemic complications [7]. Disadvantages include a higher rate of infection, seroma formation, rupture, and displacement in an acute setting. Long-term complications include rupture, infection, anaplastic implant-associated lymphoma, and capsular contracture [10]. The females have a sense of carrying something unnatural which is the most important source of patient dissatisfaction. Hence recently females are preferring autologous reconstructions [11].

BREAST RECONSTRUCTION USING FLAPS / AUTOLOGOUS TISSUE

Autologous reconstruction depends on the use of women's tissue to achieve the objective of breast reconstruction in either immediate or delayed setting [3]. Immediate reconstruction is associated with higher patient satisfaction with associated decreased overall cost. Delayed setting reconstruction is associated with inferior cosmetic outcomes, patient satisfaction, and a higher degree of graft loss due to arterial or venous thrombosis. The complication rate however is surprisingly equivalent in the immediate or delayed setting as shown in multiple studies [12].

There are numerous flap options available in the armamentarium of an oncoplastic surgeon, which includes Deep Inferior Epigastric Artery Perforator (DIEP) Flap, Superficial Inferior Epigastric Perforator Artery (SIEP) Flap, Transversus Rectus Abdominus Muscle (TRAM) Flap [3]. Other less utilized options include Transverse Upper Gracilis (TUG) Flap, Superior gluteal Artery Perforator (SGAP) Flap, Inferior Gluteal Artery Perforator (IGAP) Flap, and Profunda Artery Perforator (PAP) Flap. Lower abdominal flaps in the form of DIEP, TRAM, or SIEP are the most favored ones which will be discussed in detail. Autologous reconstruction allows a more natural, aesthetically acceptable, and durable outcome at the expense of donor site morbidity which includes scars, contour deformity, and functional impairment. Wound-related complications occur in around half of the patients suggesting their radical nature [13].

The most commonly used abdominal flaps for breast reconstruction are TRAM and DIEP [12]. TRAM is associated with fewer ischemic complications as opposed to DIEP. Pedicled flaps like TRAM are associated with bulk loss due to fat decomposition in the long run as contrasted with free flaps like DIEP, especially in obese patients [12]. This ischemic loss can be minimized over the period by neovascularization produced by a vascular delay procedure 2-3 weeks before TRAM or DIEP. TRAM, however, is associated with more donor site complications in the form of a hernia due to loss of rectus muscle. In one study it has been estimated that TRAM is associated with a rate of the herniation that is double to the DIEP. This is the reason that most experienced micro-surgeons now have started relying on DIEP flap instead of TRAM flap [3].

If the abdominal flaps are not available due to certain reasons then the thigh and buttocks are the most commonly used sites for harvesting the perforator flaps. For these perforator flaps, the most important thing is the availability of the feeding perforators at the recipient sites. Mostly the perforators of the mammary vessels are utilized. TUG flap has recently been used most efficiently to provide the bulk to the breast. TUG flap is based on a profound artery perforator supplying the Gracilis muscle and the inguinal region extending to the back [14]. It is a very common and definitive site for the perforator and readily provides bulk to the flap. A significant amount of fat can be harvested. Donor site morbidity may be quite significant and the lymphatic leak can be troublesome after harvesting this flap due to loss of lymphatics in the inguinal region.

Gluteal region flaps which include Superior Gluteal Perforator Flap and Inferior Gluteal Perforator Flap are other options. However, they require extensive expertise even in the good hands [15,16]. Loss of Sciatic nerve or posterior cutaneous nerve of thigh and donor site morbidities are the most important hurdles in their consistent use. The perforator sizes are usually small and donor site issues are quite significant including infection, contour deformity, and scar formation [16].

The success of any free or pedicled flap lies in the quality of the blood supply and it is more important to focus on it when we are utilizing the perforators which are usually smaller than the named vessels [3]. As the radiological investigations have improved, MRI and doppler are available to assess the quality and diameter of the feeding vessels which is important to know pre-operatively especially when there is a risk to perforators due to previous surgery on the anterior abdominal wall. CT angiography or MR angiography are more reliable as opposed to the hand-held doppler. These are being increasingly used in situations where we need to be sure if the perforators are available for the free flap especially following any abdominal surgery like cholecystectomy and C-section during which perforators or SIE veins and perforators are at more risk of damage. Hence, it is important to note that abdominal surgery is no absolute contraindication for the DIEP or TRAM. Pre-operative evaluation is the key before handling these difficult cases.

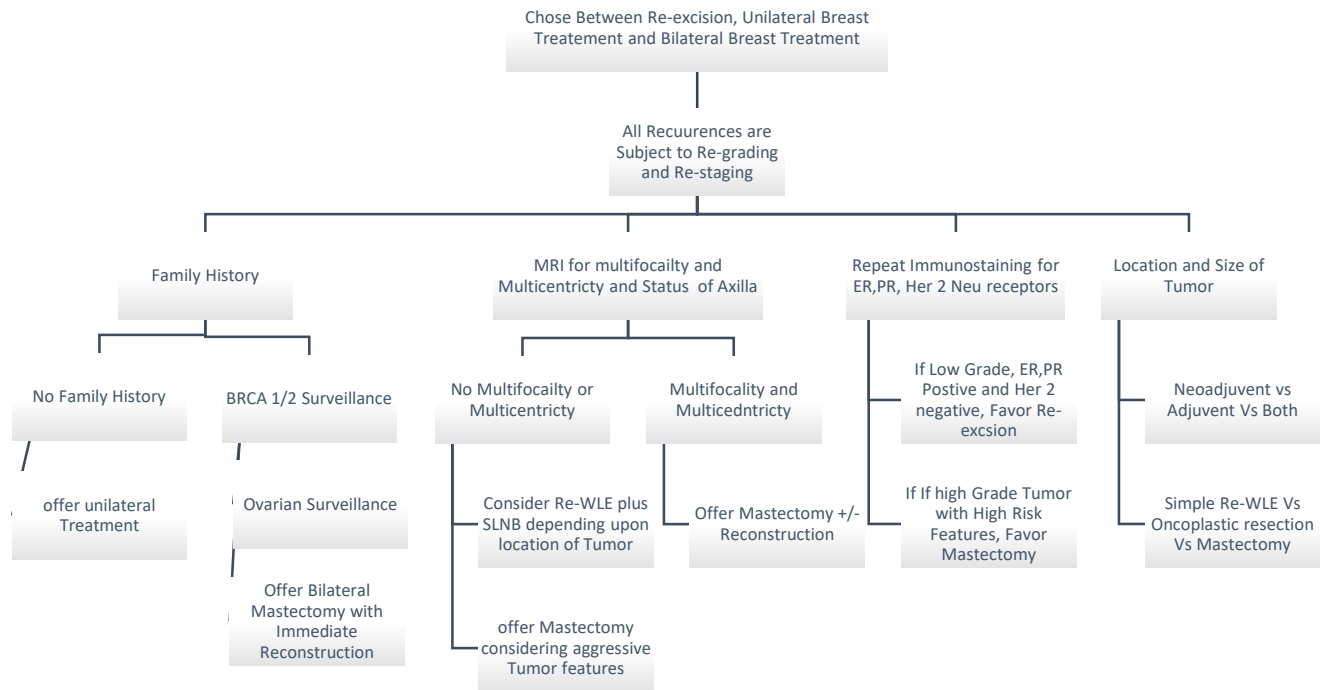### Immediate or Delayed Reconstruction?

Breast reconstruction can be done along with mastectomy in two ways either immediate or delayed [17]. The greatest advantage of immediate reconstruction is the fewer number of surgeries and low financial burden [18]. The immediate or one-stage reconstructions are better in terms of positive emotional well-being than the delayed or two-stage reconstructions. Patients with immediate reconstructions show low levels of depression and anxiety and because of positive body impression and self-concept, women are more confident and have better sexual fulfillment. A skin-sparing

mastectomy is quite suitable for the small to moderate-size breast without significant ptosis and healthy skin flaps. The bulk can be provided by the free or pedicled tissues. Single-stage methods however are associated with a higher degree of implant extrusion, flap necrosis, and higher infection rate. It is always difficult to obtain symmetry with a one-stage operation. The reconstructed breasts are usually smaller than the contralateral healthy breast.

On the contrary, the delayed reconstruction is associated with the availability of a liberal amount of time for the patient to think about the available options and it provides the surgeons to manage the patient's expectations in terms of the overall outcome of the breast reconstruction [14]. The delayed reconstruction is one of the most commonly used operative options. It can be either in the form of implant-based reconstruction or autologous reconstruction. The

implant-based reconstruction can be a single-stage if there is no fear of having postoperative radiotherapy or a two-stage procedure which comprises of insertion of a Becker's prosthesis at first intervention followed by replacement with a permanent implant [14]. The two-stage approach bridges the period for chemoradiation well and keeps the skin flap healthy and distended for future implant replacement without tight closure. The infra-mammary fold can also be conveniently adjusted in the second intervention and improves the overall outcomes of the reconstructed breast. The two-staged implant-based reconstruction is however associated with the relatively suboptimal aesthetic outcome. In case of low bulk or infection, Latissimus Dorsi (LD) muscle can function as a salvage flap [14]. Autologous flaps however are associated with the absence of implant-related complications [19].

ALGORITHM FOR ONCOLOGICAL DECISIONS

Chose Between Re-excision, Unilateral Breast Treatement and Bilateral Breast Treatment

All Recuurences are Subject to Re-grading and Re-staging

Family History

No Family History

offer unilateral Treatment

BRCA 1/2 Surveillance

Ovarian Surveillance

Offer Bilateral Mastectomy with Immediate Reconstruction

MRI for multifocailty and Multicentricty and Status of Axilla

No Multifocailty or Multicentricty

Consider Re-WLE plus SLNB depending upon location of Tumor

offer Mastectomy considering aggressive Tumor features

Multifocality and Multicedntricty

Offer Mastectomy +/- Reconstruction

Repeat Immunostaining for ER,PR, Her 2 Neu receptors

If Low Grade, ER,PR Postive and Her 2 negative, Favor Re-excsion

If If high Grade Tumor with High Risk Features, Favor Mastectomy

Location and Size of Tumor

Neoadjuvent vs Adjuvent Vs Both

Simple Re-WLE Vs Oncoplastic resection Vs Mastectomy

Radiotherapy & prosthetic breast reconstruction

Radiotherapy can have a dramatic impact on the reconstructed breast [20]. The reconstruction if avoidable, should be avoided before the radiation therapy. Radiation can affect significantly in acute and chronic settings [20]. In an acute setting, about 95% of the patients develop radiation-induced dermatitis characterized by edema, redness,

desquamation, and ulceration. In the chronic setting, it is associated with skin retraction, induration, chest and shoulder pain, and movement restriction in the neck and shoulders [20]. Radiation-induced fibrosis is permanent and is associated with Becker grade III and IV capsular contractures in case of implant-based reconstruction, in about 68% patients [20]. It would be wise to have Becker's implant during the bridging period associated with chemoradiation. If in

few circumstances, the final histopathology report following mastectomy, shows invasive cancer and lymphadenopathy then it would be prudent to tell the patient of higher chances of capsular contractures postoperatively.
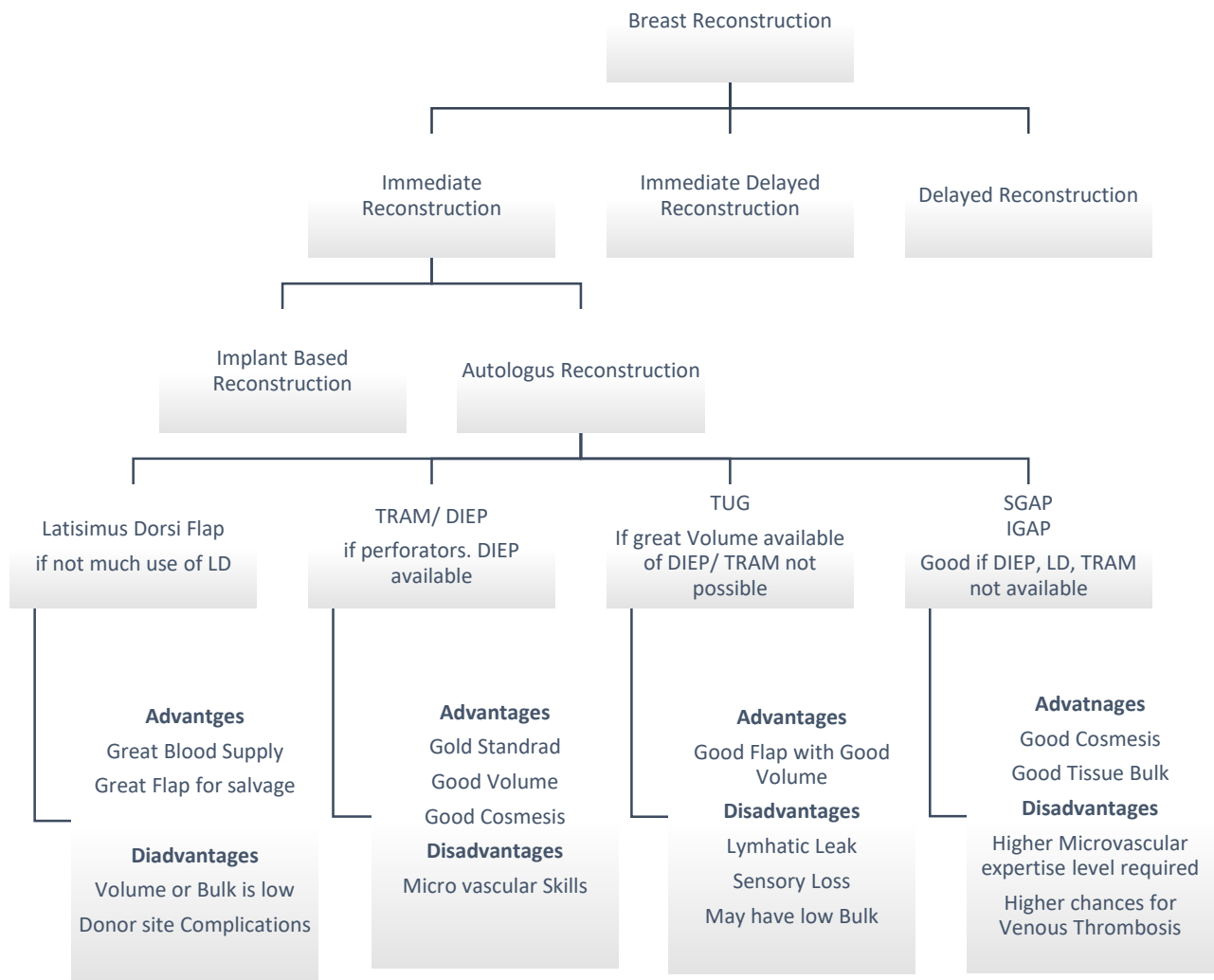
Complications associated with Implant-Based and Autologous Reconstructions

Appropriate patient selection is pivotal for the better outcomes of the reconstruction whether implant-based or autologous [21]. Various risk factors have been identified to adversely affect the reconstruction which includes the history of diabetes, increased BMI, smoking,

immunodeficiency, hypertension, certain characteristics of the body habitus, and breast characteristics [3].

Diabetes is one of the strongest limiting factors in a successful reconstruction without complications [21]. It induces hyperglycemia which is associated with poor blood supply and higher soft tissue infections. The patients need to have a blood sugar level below 200 mg/dl and urine glucose should be absent. Uncontrolled diabetes is linearly correlated with infection and reconstruction failure rates. It promotes poor wound healing and wound dehiscence [7].

ALGORITHM FOR BREAST RECONSTRUCTION

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                          Breast Reconstruction
                    ┌──────────────┼──────────────┐
              Immediate        Immediate Delayed    Delayed Reconstruction
            Reconstruction      Reconstruction
          ┌──────┴──────┐
   Implant Based     Autologus Reconstruction
   Reconstruction
                ┌─────────────┬─────────────┬─────────────┐
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Latisimus Dorsi Flap
if not much use of LD

TRAM/ DIEP
if perforators. DIEP available

TUG
If great Volume available of DIEP/ TRAM not possible

SGAP IGAP
Good if DIEP, LD, TRAM not available

Advantges
Great Blood Supply
Great Flap for salvage

Diadvantages
Volume or Bulk is low
Donor site Complications

Advantages
Gold Standrad
Good Volume
Good Cosmesis

Disadvantages
Micro vascular Skills

Advantages
Good Flap with Good Volume

Disadvantages
Lymphatic Leak
Sensory Loss
May have low Bulk

Advatnages
Good Cosmesis
Good Tissue Bulk

Disadvantages
Higher Microvascular expertise level required
Higher chances for Venous Thrombosis

Tobacco use leads to strong vascular constriction compromising the blood supply of the tissues including feeding flaps vessels and is associated with higher ischemic flap complications. The patients need to stop smoking at least 6 weeks before the breast reconstruction in most of the units [7].

Similarly, higher BMI is associated with poor reconstruction outcomes. The patients need to have BMI below 30 for any reconstruction [7]. Planned weight reductions are hence important preoperatively to handle the disadvantages of higher BMI. Hypertension needs to be controlled [7].

Patients having tissue disorders and immune deficiency need to be optimized or preferably should avoid such reconstructions [7].

Mammary hypertrophy associated with grade III or beyond ptosis is associated with the poor blood supply of the flaps hence are not good candidates for the skin-sparing mastectomy and these patients need to have reduction mammoplasties along with resection of the tumors [7].

Infections can hamper both implant-based and autologous reconstructions of the breast. Implant infection is the leading cause of reconstruction failure [7]. Pre-operative and post-operative broad-spectrum antibiotic prophylaxis is used routinely to avoid infection in these settings, otherwise, exclusion of implant or tissue reconstruction may be the rule. Extended antibiotic use should be avoided to limit the development of resistant organisms. Topical antibiotic use could reduce the contracture rates but not the infection rates.

Rates of seroma formation have been reported from 0.2-20% [7,22]. Obesity, insertion of foreign body, lymphatic destruction, postoperative inflammatory response, large dead space, and ADMs are the most common risk factors for seroma formation. Seroma may lead to higher infection rates also.

Implant extrusion and exposure is a serious complication of implant-based reconstruction [7,23]. The flap thickness in this regard is very important and the role of radiotherapy is significant. The flaps need to be thick enough to have a good blood supply and avoid ischemic complications and secondly should be able to withstand the effects of the radiotherapy which are real. Radiotherapy may lead to complete necrosis of the flap and an explanation of the prosthesis would be required in these circumstances.

Anaplastic Large Cell Lymphoma (ALCL) is one of the most important complications which have come to light recently. Various type of lymphomas has been attributed to be associated with implant-based reconstruction including T cell lymphoma, follicular lymphoma, marginal zone B cell lymphoma, primary effusion, lymphoplasmacytic type. However, these types are mostly curable [24].

CRITICAL APPRAISAL OF THE CASE SCENARIO

1.   Before devising a plan for this particular patient many questions need to be asked in history and clinical examination. It would be important to get information regarding previous oncological workup, surgical interventions, details about radiotherapy, family history, and patient aspirations and expectations about the future treatment plan. Signs and symptoms of the metastasis would require scrutiny.

o   Family history is important because a patient may be having BRCA 1/2 mutation for which she might be requiring an ovarian work up and may alter the management plan altogether. If a patient is positive for BRCA 1/2 mutations then she would be offered and possibly opting for a bilateral prophylactic mastectomy with immediate reconstruction instead of local WLE or single breast treatment.

o   The previous history of radiotherapy would make the surgeon cautious about future wound complications and the choice of local or distant flaps.

o   Similarly, the need for postoperative adjuvant radiation would also be an important determinant of future surgical interventions.

2.   On clinical examination, it would be important to know the size and location of the tumor, its relationship with NAC, and also, we need to know the clinical status of the axillary lymph nodes. It would be important to re-stage and know the current stage of the disease. Likewise, it would be important to know the size and location of the tumor if a patient opts for a breast-conserving option in form of traditional WLE or oncoplastic resection. If a patient has positive clinical nodes then metastatic workup would be required and this also shows the need for future radiation therapy in the adjuvant setting. It would also be important to preoperatively know the degree of ptosis and size of the breast. Moreover, the aspirations and expectations of the patients regarding the reconstruction need to be known and tailored accordingly in the management plan.

3.   It would also be important to re-grade and re-stage this patient. This would require the use of trucut biopsy, US, mammogram, and perhaps MRI. I would also like to immunostain the trucut blocks to know the molecular oncological features of the disease.

4.   In this particular patient it would be appropriate to do an MRI of the breast and axilla and do metastatic workup if required. If a patient has a strong family history then it would be appropriate to get genetic testing for BRCA 1/2 mutations as it would alter the decision tree.

5.   Management Options for Breast & Axilla: Patients with early recurrent breast cancer may opt for WLE again on oncoplastic resection if the disease is confined and tumor aggression is low. This may be contested by few experts however few surgeons may still have reasons to go for this

option. If the patient has high-risk tumor features on a re-work-up, it would be appropriate to choose mastectomy with SLNB. This patient is having triple-negative cancer and a grade 3 tumor, which would be better treated aggressively. However, WLE and oncoplastic resection may be feasible if the disease is limited and confined.

6. Reconstructive Options: There are many reconstructive options available. The reconstruction can be immediate, immediate-delayed, and delayed. It may be implant-based or autologous or a combination of the both. This patient has been in favor of autologous reconstruction. If the patient does not have significant use of LD flaps, then LD flaps may be utilized. Other options include TRAM, DIEP, TUG, IGAP, SGAP flaps. History of cholecystectomy and C-section is not absolute contraindications for the TRAM or DIEP. The patient may be all right to have these flaps if the CT angiogram shows good perforators and blood supply.

7. Social and Lifestyle Issues: All the flaps have pros and cons and must be carefully chosen to meet the requirements of the oncological perspectives, aesthetic outcomes, and patient desires. For example, although LD can function as a great salvage flap it may be inappropriate to go for the LD flap in patients requiring strenuous activity like dancers, swimmers, climbers, etc. DIEP is considered a gold standard in these circumstances.

8. Consent Process: Consenting process should include information regarding the failure of a flap, redo surgery, take-backs, and the complications associated with the flaps especially the thrombosis, infection, and loss rates, and the modalities that would be used in case of failure.

9. Adjuvant Therapy: Adjuvant therapy can influence the outcomes of the reconstruction and overall treatment. The postoperative need for the radiation is very important to assess before the operative intervention so that the reconstructed breast suffers the least.

10. Surveillance and Follow-up: Surveillance and follow-up differ among the patients, severity, and type of the disease, and the surgical modality used for the reconstruction.

11. Patient-Reported Outcome Measures (PROMS): Breast-Q has important measures to know the outcomes of the reconstructed breast and they should be incorporated into the practice.

12. Medicolegal Factors: Several factors are involved when planning and executing a breast reconstruction.

CONCLUSIONS

With recent advancements in the field of microsurgery, surgeons can recruit many perforator-based flaps which used to be not available in the past. The surgeons are shifting very rapidly towards the autologous route because of their increasing experience in microsurgery and also because of increasing patient satisfaction with reconstructions that are more natural and acceptable. DIEP and other perforator flaps are rapidly replacing TRAM because of the higher incidence of herniation. TUG, SGAP, and IGAP are other acceptable alternatives but they require more expertise. For choosing any flap pre-operative evaluation of the donor's vessels through CT angiography or color doppler is important. Microsurgery skills would be of pivotal importance in the future for reconstructions. Implant-based reconstruction still is quite effective and popular. Nipple and skin-sparing mastectomies have shown great promise to immediate breast reconstructions especially in cases of DCIS or for cancer prophylaxis. Anatomical and rounded implants can be individualized to the demands of the patients. Anaplastic implant-associated lymphoma needs careful research and scrutiny in the future. Oncoplastic resections can also be an important alternative to reconstructions and have been recently advocated by many with good oncological safety principles and aesthetic acceptability. The treatment plans in the future have to be individualized or personalized according to the needs and demands of the patients.

ARTICLE INFORMATION

Author Affiliations: Department of Surgery, Shalamar Medical & Dental College, Lahore, Pakistan (Ahmed, Ahmed, Zaib)

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Archives of Surgical Research | How I Do It?

Clinical And Biomechanical Basis Of Implant Based Breast Reconstruction

Mubashir Cheema, Sairah Naseem

IMPORTANCE Breast cancer is one of the most common malignancies around the world. In a developing country like Pakistan the patients may present late or be unreliable/irregular in follow up. Hence mastectomy and implant based reconstruction are a typical form of management. Our aim is to summarize the principles of patient assessment, types of breast prostheses their common indications as well as the limitation of implant based breast reconstruction.

DISCUSSION Ability to deconstruct the defect in smaller subunits (e.g. using the "three step principle") helps understand the defect and plan appropriate management for any breast defect. Management starts with choosing an appropriate type of prosthesis. Physical dimensions of the implant are chosen to achieve symmetry with the contralateral side (or an idealized shape, in case of bilateral reconstruction). Different implant characteristics may be chosen to "fine tune" the reconstruction to the individual patient. The technique however, does has its limitations.

CONCLUSIONS Implant based reconstruction is just one tool in the surgeon's toolbox to manage defects resulting from resection of breast cancer. A knowledge and competence in all possible options can help the surgeon individualize management for each of their patients.

KEYWORDS Breast, reconstruction, implant, prosthesis, expander, Becker

How I Do It?

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author:
Mubashir Cheema FRCS(Plast), EBOPRAS, MRM
Department of Plastic Surgery, University Hospitals Birmingham, UK
mubashir.cheema@nhs.net
+44 121 371 2000
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Breast cancer is one of the most common malignancies in women, affecting an estimated 2.3 million per year[1] around the world. Its management depends on the histologic type and clinical stage at the time of diagnosis. This, in turn, determines the final size of the defect after any tumor extirpation. The physical size of this defect and its proportional relation with the breast size factor in to the decision for breast conservation surgery (BCS) vs mastectomy. The reconstructive options, especially in developing countries take in to account the patient and the surgeon characteristics. Due to a combination of poverty, illiteracy, misconceptions and long distances involved in reaching surgical care, the patients may not return for multiple follow-up visits. While there are autologous and prosthetic options possible for a given patient, the surgeon may not be well versed in autologous reconstruction and/or may wish to keep the surgical option as simple as possible, in view of patient characteristics.

Our aim is to summarize the principles of patient assessment, types of breast prostheses their common indications as well as the limitation of reconstruction using prostheses.

Principles of assessment: A simple reproducible way to assess the defect involved is to deconstruct the breast shape in to simpler ones and compare them with contralateral (or to the intended result). Blondeel at al.[2,3] have described this as a "three step principle" that assesses the so called foot plate, conus and the envelope (Figure 1).
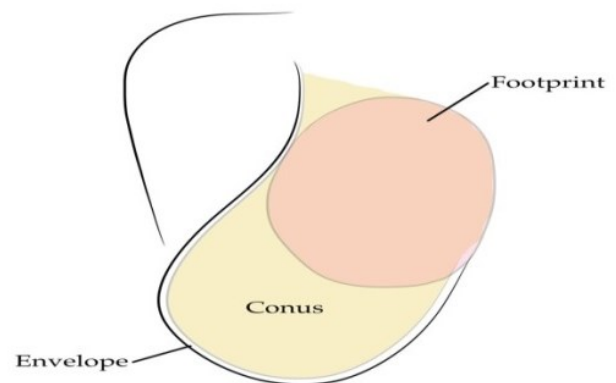
Figure 1: Three step principle deconstructs the shape of Breast to a footplate, conus and envelope to allow assessment and decision making about each part independent of the other.

Foot plate (also known as the 'Base') is the imprint of the most proximal part of the breast on to the chest wall. It has been classically described as extending from 2nd to 6th intercostal space in vertical dimension and from anterior axillary line to parasternal in horizontal dimensions. The foot print is relatively consistent, with exception of congenital anomalies of development or tubular breast deformity. The "envelope" refers to the skin covering of the breast tissue

and may be thin or lax. Due to the skin's viscoelastic properties (i.e. it is prone to stretch), it cannot provide lasting shape to the breast tissue by itself. In contrast, the "conus" represents the volume of breast parenchyma, and does not include the skin. The distinction between envelope and conus becomes important in immediate vs delayed breast reconstruction.

Mastectomy patients in whom immediate breast reconstruction is contemplated, the native skin envelope is preserved as well as the foot plate. The only thing needed is the volume of the breast conus, which can be provided with autologous tissue (i.e. pedicled or free flap) or using synthetic material (i.e. a definitive implant).

In delayed breast reconstruction, all three features are missing. While the foot plate (or base) can be copied from the contralateral side, the conus and the envelope present a challenge. While autologous reconstruction (with pedicle or free flap) can bring in both volume as well as extra skin at the same operation, implant based reconstruction cannot provide both at the same time, hence we need to place a tissue expander to "create" extra skin for the envelope over a period of time. Once the skin envelope is large enough, the expander is replaced with a definitive implant. Note that due to thin skin, the final shape of the breast follows from the shape of the implant placed. This of course has its limitation that it can only match the volume but it cannot reproduce natural ptosis which may exist on the contralateral side. (In such a situation, one option may to perform a symmetrising procedure to shape the contralateral non-diseased breast to match the ipsilateral reconstructed side. However, this option, of placing scars on an otherwise healthy tissue, may not appeal to every patient).

Types of Prostheses: Prostheses used for breast reconstruction may be a tissue expander (also called breast expander), a definitive prosthesis or an expander-implant (also called Becker prosthesis).
1) Tissue/ breast expander is a medical device consisting of a shell of silicone polymer that is placed in sub-pectoral (or more recently, pre-pectoral) space in patients needing delayed breast reconstruction. The expander is regularly topped up with saline through a remote or integrated "port" to increase its volume. The increase in volume also increases its surface area which recruits as well as stimulates the growth of new skin via the process of tissue expansion.

2) Definitive prosthesis has a silicone elastomer shell and is filled with either saline or silicone polymer (different in composition from that of the shell). In contrast to an expander, the volume of a definitive prosthesis is fixed and cannot be changed.

3) Expander-implant, also known as "Becker implant" have a silicone shell but the inside consists of two separate chambers. In one chamber is a certain fixed volume of

silicone polymer, and the other is potentially empty but can have a variable amount of saline injected in to it through an attached port.

Characteristics of a definitive breast implant:
(A) Fill
An implant may be filled with saline or silicone, making it a saline or a silicone implant. Saline implants are possibly only used in some places within the USA. We think that it is due to the historical "silicone controversy" of the 1990s when FDA placed a moratorium on silicone breast implants[4]. However, since then several studies confirmed the safety of silicone implants against concerns cited in the original controversy[5].

Silicone gels of different viscosities (also called cohesiveness or cohesivity) have been developed over the years. Less viscous gels are considered softer to touch but increase the tendency of "rippling" (i.e. any unevenness of the implant surface may be visible through the patient's skin) . Implants with softer gels are more likely to lose shape in case of implant rupture or physical damage to the implant shell.

(B) Surface
One of the most common sequelae of breast implants is the formation of a fibrous capsule, called capsular contracture (CC). Histologically, it consists predominantly of fibroblasts and myofibroblasts. Clinically, it grows slowly over time and can make the breast feel firmer over a period of many years. After any radiotherapy for breast cancer, there is increased risk of developing an excessive capsule ("adverse capsular contracture")[6,7] which in addition to making the breast firmer, can make it contracted/misshapen or even painful[8]. The myofibroblasts in the adverse capsule are more likely to be aligned in one direction, therefore providing a cumulative force of contraction.

To counteract this effect, textured implants were developed where the surface has microscopic irregularities, in order to try to reduce the net vector of contraction by the fibroblasts[9]. The current surface technologies available are the Siltex™ "microtextured" surface by Mentor Inc. (J&J, USA) and the nanotextured surface by Motiva implants (Establishment Labs, Costa Rica). The difference between micro- and nano-textured surfaces is the size of the surface irregularities.

While fibroblastic response to radiation accounts for post-radiotherapy capsule formation, many patients develop adverse capsules in absence of local irradiation. Various factors have been implicated in this situation, all of which result in a limited sub-clinical inflammatory process that continues to produce fibroblasts over a continued period of time. The most important of these processes is sub-clincial infection with Staph epidermidis[10]. Other factors include tissue injury from blunt dissection or fibrosis resulting from any small hematoma or foreign material. This foreign material may be microscopic debris on surgical gloves, latex

microparticles from gloves, desquamated skin cells from adjacent to the wound, electrocautery products retained in the dissection pocket, or dust particles from the theatre environment attracted by electrostatic charges created by friction between implant and its environment before implantation.

Therefore some surgeons[11] recommend a set of precautions at each operation involving implant insertion. These include:

1. covering nipple areola complex in the surgical field with clear adhesive dressings (e.g. Tagaderm™)
2. using sharp atraumatic dissection using electrocautery (facilitated by surgery under direct vision)
3. active extraction of electrocautery fumes
4. change of gloves for insertion of each implant, as well as re-prep of the surgical field (with aqueous antiseptic)
5. instillation of an aqueous antiseptic / antibiotic solution in the implant packaging before its removal (to deliver antibiotic and to minimise any electrostatic attraction of dust particles on to the implant)
6. thorough washout of implant pocket to remove any debris
7. instillation of the implant cavity with antibiotic or antiseptic solution (see below)

There is no consensus in the choice of antibiotic/ antiseptic but combinations range from a single agent (e.g. betadine), two agents (e.g. gentamicin-cephalosporin) or three agents (e.g. an antibacterial-antiviral-antifungal combination). The senior author (M.C.) in his aesthetic practice, uses all the above steps with clindamycin as his choice of antibiotic for instillation. With respect to time taken, we find that with some practice all these steps can be performed swiftly and do not impact overall surgical time.

(C) Shape
A definitive breast implant may be round or anatomical in shape. While the round implants may have a smooth or textured surface, majority of anatomical (also called 'shaped') implants have a textured surface. The exception being the TruFixation™ anatomical implants by Motiva (Establishment Labs, Costa Rica) which have a nanotextured surface and use tabs to suture the implant in place.

There has been a long standing debate about the merits and demerits of each implant shape. Those preferring round implants point to the perceived lack of aesthetic benefit and a certain rate of rotation of the anatomical implants. In the senior author's (M.C.) opinion, the final shape of the breast is determined firstly by the thickness of the soft tissue and then by the underlying implant, i.e. if the soft tissue cover is thin (e.g. most cases of implant-only breast reconstruction) the final shape is determined by the underlying implant[12,13].

But if the soft tissue cover is thick (e.g. a pedicled latissimus dorsi flap) the final shape of the breast is less dependent on that of the implant. In general, anatomical implants are important in cases where a more natural final breast shape is desired, or where there is need for preferential expansion of the lower pole (e.g. in tubular shaped breasts). The anatomic implants are generally more expensive than the round ones.

(D) Dimensions
The chosen implant needs to respect the anatomical landmarks. So it must not breach the boundaries of the foot plate discussed above. This leaves the projection and the choice of implant shape as the determining factors for the final breast shape. A round implant's most projected point is the center of its vertical dimension (i.e. diameter). Aesthetically, that places it well above the existing (in case of IBR) or new (in case of DBR) infra-mammary fold. The most projected point of the anatomical shaped implants is relatively lower in its vertical dimension, which alongside the tear drop shape, can give the final result a more natural shape. However, neither implant shapes can reproduce a ptotic look on their own, which is a limitation of breast reconstruction by implants only.

(E) Volume
The final volume is dependent on the physical dimensions of the implants, but also on the implant shape. Anatomical implants for the same base dimensions and projection, have less volume in the upper pole and therefore have less total volume and are lighter than round implants. Some surgeons emphasize volume as the primary measurement unit for the choice of implant which, in our opinion, misses the opportunity to plan reconstruction using physical dimensions of the base plate.

How to choose and position an implant:

Several methods have been described to allow surgeons to choose an implant for aesthetic breast surgery. Of these, the two most commonly cited methods are those by Per Hedén[14,15] and John Tebbetts[16]. In turn, these methods have been adapted for use in implant based breast reconstruction.

1. Implant shape is chosen based on the desired result and available soft tissue cover.
2. The dimensions of the contralateral footplate are copied (assuming they are within an acceptable range of dimensions described as "normal). The thickness of ipsilateral soft tissues needs to be subtracted from this measurement to obtain the possible base-dimensions of the required implant. The simplest clinical measurement of the soft tissue contribution is the "pinch thickness" at that point (measured by gently pinching the tissues between the examiner's thumb and index finger). The pinched tissue consists of two layers of skin and soft tissue (Figure 2) Hence the soft tissue

thickness is half of this pinch thickness. Thus half of the local pinch thickness at medial and lateral extents is subtracted from the width of the footplate to get the maximum implant width/diameter. In case of anatomical implants, a similar calculation can provide the maximum height as well.
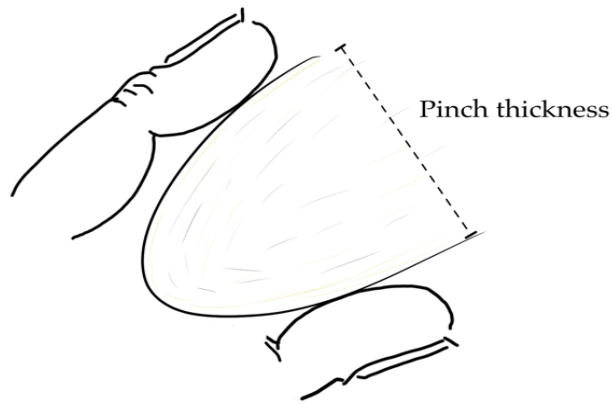
Figure 2: Skin pinch is a quick clinical measurement as half of skin pinch ("half skin pinch") is the local tissue thickness. The half skin pinch is measured at both medial and lateral extents of the breast. The sum of these values is the tissue contribution to the breast width. Subtracting this tissue contribution from the measured breast width is the maximum allowable width/diameter of a breast prosthesis.

3. Once the shape and base dimensions have been decided, then choosing either the projection or the volume completely specifies the implant. Tebbetts[16] described a clinical method to estimate the implant projection in aesthetic breast surgery by anterior translation of the NAC. However, the senior author (M.C) finds some elements of this method unreliable and prefers instead to list a range of options of implant volume and projection for the patient. The patient tries out these different sizers in clinic (and possibly at home too, using a fillet made by pouring a known volume of rice in a plastic bag- the "rice-bag test").

Once chosen, the implant is placed so that an ideal NAC (constructed later, using local flap, or tattooing) is positioned in the breast meridian and that approximately 60% of the resultant volume is below the NAC[17] (Figure 3).

Pros and Cons of implant based breast reconstruction:
Implant based breast reconstruction is sometimes considered a short, quick-fix operation but it poses more issues in the long term. If the patient needs radiotherapy, there is higher risk of skin break down and adverse capsule formation. The already thin skin and an adverse capsule can compromise the aesthetic outcome. Even in best of situations, the breast reconstructed with implants looks different from contralateral, has limited ptosis and does not droop over time as the contralateral one thus leading to increasing asymmetry. There are further concerns about risk of implant rupture and BIA-ALCL[16]. At the end of all this, it only provides volume symmetry for the patient, which may appear acceptable in clothes.
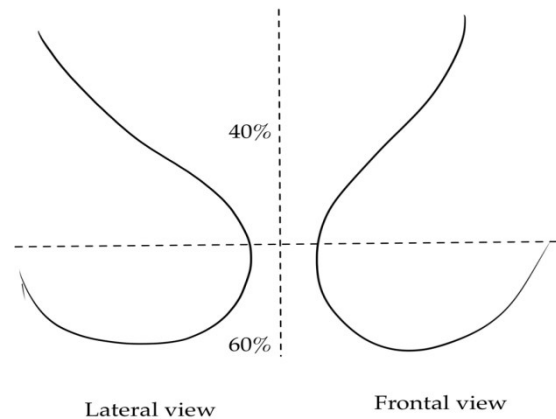
Figure 3: 40% of breast tends to be above the nipple and approximately 60% is below it. Although there is discrepancy as to whether it means volume or height of the breast (The ratio was first measured as height on photographs, but more recently has been used to describe volume as well). Sometimes an alternative ratio of 45:55 is used instead. In practice, the difference is only a few millimeters.

CONCLUSION

In our opinion, breast reconstruction surgery needs to be individualized to the patient by offering all modern surgical options. While implant based breast reconstruction is suitable for some patients, it is just one tool in the surgeon's toolbox and should not be considered as the only solution for every patient.

Author Affiliations: Department of Plastic Surgery University Hospitals Birmingham, UK

Conflicts of Interest: There are no conflicts of interest

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Archives of Surgical Research | Short Communication

Anaplastic Large Cell Lymphoma In A Patient With Breast Implant (BIA-ALCL): An Extensive Review

Mahpara Nawazish, Sana Iqbal, Irfan Saeed, Ubaid Ur Rehman

IMPORTANCE Breast implant associated with anaplastic large cell lymphoma (BIA-ALCL) is a newly diagnosed non-Hodgkin lymphoma. This is a variant of T cell lymphoma and a rare disease but its increasing use in patients with breast implants after mastectomy makes it more challenging for the whole of the world. The exact pathogenesis has not been explained so far. It generally appears as a unilateral effusion limited to the capsule of textured implants. BIA-ALCL tends to form a mass that spreads regionally through the capsule into surrounding tissues and then from soft tissues to lymph nodes. Unlike other non-Hodgkin lymphomas, in BIA ALCL surgery is a mainstay of the treatment and it includes removal of capsule and implant at an early stage (stage I and II). For advanced stages, III and IV, adjuvant therapy including chemotherapy, radiation therapy, and brentuximab vedotin is used. The basic theme and aim of our review article are to provide precise information available on BIA- ALCL including its prevalence, pathogenesis, clinical findings, imaging, an algorithm for treatment, and recent international recommendations on BIA-ALCL. By this review, we want to increase the understanding and bring awareness to the practitioner's community about BIA-ALCL.

KEYWORDS Breast implant-associated anaplastic large cell lymphoma, breast implants, lymphoma

Short Communication

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Mahpara Nawazish, Department of Surgery, Shalamar Medical & Dental College, Lahore, Pakistan
mahpararajpoot123@gmail.com
092-306-0657757
https://doi.org/10.48111/2021.03.07

A naplastic large cell lymphoma (ALCL) is usually CD30 positive and is a type of T-cell non-Hodgkin lymphoma. They are subdivided based on anaplastic lymphoma kinase (ALK) ALK-positive and ALK-negative and primary cutaneous ALCL which have the same histology but divided into different clinical groups.[1] Breast implants are divided into three categories. Firstly based on components such as saline and silicone gel-filled, secondly on the surface (textured surface and smooth surface), and thirdly on configuration into symmetric and non-symmetric.[2] Worldwide, almost 1.5 million women underwent breast implants surgery every year, out of which nearly 4.5 million implants were done in the United States of America. The main purpose of breast implants is to augment and reconstruct the breast in patients following mastectomy.[2] "The first case of BIA-ALCL was reported by Keech and Creech in 1997", and studies revealed that BIA-ALCL has a strong association with a textured type of implants. The exact mechanism is still unclear.[3][4] In 2008, a Dutch study reported a positive link between BIA ALCL and breast implants by using its vast data collected from different countries on pathology, that described various forms of breast pathologies.[3,5] When classic systemic ALCL and BIA ALCL compared; there were two pathological types recognized. One is the seroma type that was most common and the second was the mass type that was less common but

aggressive in nature.[6] In the early postoperative period, the chief complaint is effusion around the implant and can be associated with sepsis, non-specific inflammatory reaction, and hematoma formation. The presence of effusion more than 1 year after implant surgery is uncommon, approximated to be less than 1 %. Any deferred "seroma" formation should raise the doubt of BIA ALCL. [7]

EPIDEMIOLOGY

"The first case of ALCL in a patient with breast implant was reported by Keech and Creech in 1997". [3] Of all extranodal Non-Hodgkins lymphoma [NHL] Only 1% are non-Hodgkin's lymphomas of the breast and 0.7 % of all breast cancers.[8] B-cell lymphoma are most common NHL but T cell variant is found in 10%.[7] Post breast implantation, patients can present with the symptoms of BIA ALCL after a minimum of 3 months to a maximum of 25 years.[8]

PATHOPHYSIOLOGY

The mechanism of BIA-ALCL remains uncertain. In the literature, three theories have been proposed, based on antigen stimulation response, bacterial biofilm, and JAK/STAT pathway.[9] According to the first theory, textured

implants have more surface area which incorporates more bacteria that induces inflammatory response through macrophages, interleukins II and VI and T type cells stimulation which leads to antigens stimulation response, inflammation, immune response, and cell proliferation that alters the genetic makeup and ultimately the formation of lymphoma.[9] Second theory postulated that early investigations identified a gram-negative bacillus, Ralstonia pickettii, in establishing a subclinical, peri-prosthetic biofilm, leading to a lipopolysaccharide (LPS) endotoxin-induced carcinogenesis. After a more careful examination, the Ralstonia data have since been refuted, and currently, no clear association between the breast microbiome and BIA-ALCL pathogenesis exists.[10] The third theory suggests that the presence of an uncommon activating variant of JAK3 (V722I)may have provided a hereditary inclination. However, the joint JAK1/JAK3 mutations are very much indicative of co-occurrence of acquired mutations in STAT 3 and JAK 1 in the same tumor in patients with ALK-negative systemic ALCL, which showed its selective advantage of a synergistic effect of combined mutations. Further concentrates for a huge scope expected to decide the frequency of JAK1/STAT3 transformations in BIA-ALCL as well as genetically predisposing factors.[11]

CLINICAL FEATURES

Around 96% of the patients present with local symptoms such as pain, redness, alteration in the shape as well as size, lymphadenopathy, and breast skin lesions. While only 9% of the patients present with systemic symptoms like fever, night sweating, weight loss, and non-breast skin lesions. Most patients came with a presentation of seroma and 15% with breast masses. Majority of the patients present with unilateral involvement and only a few patients present with bilateral BIA ALCL.[12] The mean time interval of developing breast lymphoma is almost 10 years after breast implantation following mastectomy. Seroma formation is found in around 60% of patients, while with a mass the ratio is 17% and combined seroma and mass presentation are found in 20% of the population.[13] Factor that increases the risk of developing BIA ALCL are obesity, genetics, and history of autoimmune disease, certain races, or ALCL in other sites.[14]

HISTOLOGICAL FEATURES

On histology of seroma, malignant cells are appreciated on cytology and cell block preparation. After capsulectomy, mostly tumor cells are aligned at the luminal side of the fibrous capsule, entrapped in the fibrinoid network, which can vary in distribution patchy or focal distribution. In patients presenting with the mass lesion, the malignant cells appear in the form of bundles and sheets mixed with eosinophils along with necrosis and sclerosis.[15] Tumor cells are variable in size and shape, having a high mitotic count

with hallmark cells that are common in all types of ALCL. The cells may some of the time have eccentric bean-shaped nuclei, multinucleated, and look like Reed–Sternberg cells.[16] The diagnostic board should incorporate B cell markers (CD20, CD79, PAX5) and EBV to prohibit other huge cell lymphomas [diffuse huge B cell lymphoma (DLBCL) and classical Hodgkin lymphoma (cHL)]. A pan-cytokeratin to rule out poorly differentiated carcinoma, and S100 and Melan-A to eliminate melanoma, are additionally fundamental in this setting.[16] "They are strongly positive for CD30, sometimes for CD43, often positive for the cytotoxic markers TIA-1, granzyme B, and perforin Tumor cells are negative for Epstein-Barr virus (EBV) and ALK".[15]

IMAGING STUDIES

Imaging studies of BIA-ALCL may show an effusion and mass. "Adrada et al studied the sensitivity and specificity of different imaging modalities used for detection and differentiation of BIA-ALCL".[17,7] The ultrasound was considered a gold standard test in the detection of seroma which was 84% sensitive, and 75% specific. Magnetic resonance imaging (MRI) had 82% and 50% sensitivity and specificity respectively for effusions. PET/ CT was the most commonly used modality to detect tumor mass. Another useful screening modality for breast carcinoma is mammography, and had poor sensitivity for effusion detection around a breast implant, at about 30%.[17]

DIAGNOSIS

Tools that are helpful for diagnosis of BIA-ALCL include a detailed history, physical examination, imaging[ultrasonography, Magnetic resonance imaging(MRI), Positron emission tomography(PET)/Computerized tomography (CT)] and biopsy for cases with breast or axillary masses and nodal metastasis. To rule out BIA-ALCL aspiration of 50 to 1000 mL is advised. Send aspirate for further evaluation (culture and sensitivity, flow cytometry, and immunohistotyping for CD30 and other T cell markers) flow cytometry, and immunohistochemistry. For indeterminate cases, follow-up after every 3 to 4 months is recommended. PET/CT helps to describe the spread of lymphoma in patients with lymph nodes involvement.[2]

PREOPERATIVE EVALUATION/STAGING

For BIA-ALCL, two systems of staging are used. One is the TNM staging system and the other is the Lugano modification of the Ann Arbor staging system. Later was previously been used for non-Hodgkin lymphoma. In this system, stage IE disease is limited to the breast or implant capsule, In this stage, IIE disease is spread to or involves local lymph nodes.[2] Most patients have early-stage disease, that

is stage IE (83%–84%) or stage IIE (10%–16%), while a few of them (0%–7%) fall into stage IV disease with this system. The major drawback of the Ann Arbor staging system is that it does not describe capsular invasion. Now the TNM staging system modeled is currently used for BIA ALCL staging after the American. However, the "TNM classification describes BIA-ALCL as a spectrum of disease from stage IA (35%–70%, effusion only), IB (3%–11%), IC (8%–13%), IIA (8%–25%), IIB (3%–5%), and III (3%–9%) to IV (1%–2%)".[18] This staging system is much more oppressive in terms of event-free survival and more precisely depicts overall survival in contrast to Ann Arbor classification, and is therefore suggested now a days.[16]

TNM Staging System

T: Tumor Extent	
T1	Limited To Effusion Or Luminal Side Of Capsule
T2	Early Capsular Invasion
T3	Cell Sheets Infiltrating The Capsule
T4	Lymphoma Spread Beyond The Capsule
N: Nodal Extent	
N0	
N1	
N2	No Involvements Of Nodes
	One Local Lymph Node Involvement
	Various Local Lymph Nodes Involvement
M: Metastasis	
M0	
M1	No Distant Spread
	Spread To Different Organs
STAGES	
A	T1N0M0
IB	T2N0M0
IC	T3N0M0
IIA	T4N0M0
IIB	T1-3N1M0
III	T4N1-2M0
IV	Tanynanym1

TREATMENT

Surgical Management: The management is based on early diagnosis, complete excision, and removal of the mass and the adjoining area involving the capsule of the implant is the basic step. Radical mastectomy has no significant role in the management of BIA-ALCL because this is not a pathology of breast tissue. In more than 80% of the patients, the disease is localized to the capsule so only Surgical removal is effective.[1,10] Biopsy of lymph nodes that are enlarged pathologically may be required at the time of surgical resection. The recurrence of BIA-ALCL does not appear to be

lessened even after full axillary nodes dissection. About 4.6% of patients have had bilateral capsular involvement, removal of the textured type breast implant on the contralateral side is also suggested.[3] A flap surgery is a new convenient and emerging method in which a type of tissue is taken from the donor site and attached to the recipient site with intact blood circulation. An analogous fat grafting is another useful method for cosmetic purposes.[3] The implant capsule should be removed completely since the remains of the scar capsule increase the risk of disease recurrence. The role of adjuvant therapies like radiations is important in case of incomplete resection. For a localized disease that is not disseminated, complete removal by surgery gives good results with the majority of patients remaining disease-free for a longer duration.

Adjuvant Therapy: Adjuvant therapy (radiotherapy, chemotherapy, and brentuximab vedotin) are useful for patients with incomplete resection, local recurrence, and nodal metastasis.[1] Localized radiation (24-36 Gy) followed by surgery is helpful in patients with a localized disease where complete excision is not possible.[1,19]

Survival Rate: Prognosis of breast implant ALCL is better when contrasted with systemic ALCL.[17, 14] when a tumor is confined to the capsule the prognosis is good as compared to the tumor that invades the capsule and surrounding tissues. Specialists strongly oppose that the prognosis is worse in patients who have a history of breast tumor or lymphoma.[14]

DISCUSSION

The World Health Organization (WHO) categorized BIA ALCL and described guidelines for management in 2016.[18] Breast augmentation and implantation surgery has been increasingly used over the world since the first augmentation procedure done in 1962.[18] Low frequency of this infection itself, assessed at 0.1 per 1 lac population every year, makes it particularly hard to predict the link between lymphoma and breast implants.[20] Various triggers have a role in the development of BIA ALCL, including mechanical grafting, implant materials leaking into invading tissue, and bacterial growth. In option, an intensive appraisal of the effect of JAK1/STAT3 pathway changes may provide extra understanding in the mechanism of BIA ALCL, just as immediate helpful procedures for its treatment. Progressing and future examination on the atomic components basic BIA-ALCL may give better choices to its anticipation and treatment in all patients.[21] Now treatment with brentuximab vedotin which is an antibody-drug conjugated to a chimeric CD30 gives excellent results and considers the first line of treatment. Since 2011, the FDA has found a way few ways to all the more likely comprehend this issue, incorporating a top to a bottom survey of post-approval study information,

medical reports, logical writing, breast implants associated registries, and public conversations. In March 2019, the FDA examined many breast implants related concerns and worries in a public warning board of trustees meeting.[22] In October 2019, the FDA delivered a draft direction submitting various proposals to help women approach breast implants advantage and hazard data.[22] The FDA has prompted medical services suppliers and embed makers to report affirmed instances of iALCL through "Med Watch: The FDA safety information and adverse event reporting program.[23] In July 2019, the FDA-refreshed information base announced 573 instances of BIA-ALCS, with 116 new cases and 24 new deaths worldwide since the past correspondence in March 2019 and suggested a deliberate review of Bio cell items in the USA.[23] Doctors ought to be urged to report their involvement in brentuximab vedotin for BIA-ALCL to a repository like the PROFILE (patient registry and result for breast inserts and anaplastic large cell lymphoma etiology and the study of disease transmission) vault to permit alteration of proof-based rules for this phenomenal illness.[23]

BIA-ALCL is an unusual category of CD30- positive. T cell type lymphoma is usually developed with a textured type of breast implant almost ten years after its implantation. The diagnostic modality of choice to evaluate a delayed onset seroma is ultrasound. Surgical excision should consider in all cases. Recent studies identified aberrant JAK STAT3 pathway involvement which may serve as a therapeutic target for JAK-STAT inhibitors in the future. The revelation of BIA-ALCL presented significant and clinical worries that ought to be incorporated in the consideration interaction for a lady that chooses to go through breast implantation. Consequently, it is important to design a bunch of shrewd suggestions for oncologists and patients meant to build information about the danger and the medicines accessible. An absence of itemized data may prompt negative feelings lessening imperfect choices and diminishing consistency with the consideration. All nations and government organizations ought to advance mindfulness bringing campaigns up in request to sharpen the doctors for a legitimate cognizance of this novel illness element. To the end, more studies are needed to further delineate the most effective therapeutic regimens in the case of disseminated disease.

CONCLUSION

Author Affiliations Department of Surgery, Shalamar Medical & Dental College, Lahore, Pakistan

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Archives of Surgical Research | Perspective

Autologous Breast Reconstruction - A Brief Overview

Asif Zubair Bhatti[1], Muhammad Jibran Rabbani[1], Sania Ahmad[1], M Waqas Mughal[1], Ahmed Shehzad[1]

IMPORTANCE Breast reconstruction is one of the procedures in which detailed planning is needed to plan the surgery. The ultimate aim in the reconstruction is to achieve symmetric breasts. Both immediate and delayed reconstruction can be warranted in the cases and the result of delayed reconstruction is normally accepted well by the patient. There are two types of autologous reconstruction pedicled and free flap reconstruction. Lattisimus Dorsi Flap and TRAM flap are one of the best-known types of autologous reconstruction. The other flaps known are the SIEA flap, Rubens flap, and deep circumflex iliac artery (DCIA) flap.

KEYWORDS Breast Reconstruction, Autologous Breast Reconstruction, DIEP Flap, Latissimus Dorsi Flap, SGAP Flap

Breast reconstruction is an integral part of the overall treatment of breast cancer patient.The reconstructive surgeon should be present on the initial consultation for decisions about primary treatment of the breast since the patient may want to know what her options are? Aesthetics plays a vital role in final decision making, and if immediate reconstruction is considered, careful coordination is critical. If delayed reconstruction is to be done, the plastic surgeon can advise on placement of the incision and drains, preservation of the pedicles, etc.[1]

Cancer fear and fear of death are real concerns for the patient as well as loss of femininity and a desire to return to normal. Usually, a decision to opt for reconstruction indicates positivity and acceptance by the patient. The challenge lies not just in dealing with the patient but also in matching the correct technique with the patient's needs. The ultimate aim is to provide the patient with an aesthetically pleasing breast. Symmetry is an important consideration, and the other breast serves as a reference guide.

There are certain advantages of early reconstruction, including better recovery and rehabilitation with a reduced number of operations and admissions. Aesthetics are often easier to work with and pedicle already exposed during the surgery. However, there are some disadvantages like high patient expectations and higher incidence of wound complications.

Delayed reconstruction allows better prognostication and consideration of oncological, psychological and aesthetic factors. In patients who are to receive adjuvant therapy, Bostwick recommends waiting for 2-3 months after completion of therapy before reconstruction. This allows blood count to return to normal and strength to be regained. Also, patients tend to gain weight during chemotherapy, and this may affect the final outcome ,the modern indications for delayed breast reconstruction are either if the surgical capabilities are not available or if the histologic result will change the operative plan..[2]

When deciding the deformity, the surgeon needs to consider skin amount, quality, scar, radiotherapy damage and also examine thoroughly the anterior axillary fold and axillary roll along with pectoralis muscle status. It is imperative to examine the opposite breast: size, shape and ptosis. Main advantage of autologous recon is that, if available, it is the body's own tissue so changes proportionally with time and is better tolerant of radiotherapy. The size and volume is determined by the contralateral breast (assuming the patient is happy with it). Pedicled vs free flap is based on available surgical expertise. The exact flap is determined by available tissue at each donor site (and patient's preference of scar position).

TYPES OF AUTOLOGOUS FLAP

There are two types of autologous flap; pedicled and free flap. Pedicled flap includes Latissimus dorsi, transversus abdominis myocuteneous flap (TRAM)(unipedicled or bipedicled), Free flap included gluteus fasciocutaneus flap (superior or inferior gluteal pedicle), lateral transverse thigh flap, Ruben's flap (love handles based on deep circumflex iliac artery),free TRAM,free deep inferior epigastric artery perforator flap (DIEP flap) and free superficial inferior epigastric artery (SIEA) flap. Autologous reconstruction can be combined with the use of prostheses like breast implant or two stage expander-implant procedure.

To decide what sort of reconstruction is needed, take into consideration the patient fitness, laxity and thickness of remaining skin, condition of pectoralis major & serratus muscles,size of opposite breast,availability of flap donor site, radiotherapy, stage of disease, paitent's wishes, patient's health, body habitus and need for adjuvant therapy. Commonly, Lattisimus dorsi flap is used for medium-sized defects and for larger defects, pedicled or free TRAM or DIEP flaps are used.

I.   Latissimus Dorsi Flap

The latissimus dorsi musculocutaneous flap is type IV flap, according to Mathes and Nahai, and has a dominant blood supply from thoracodorsal artery having a pedicle length of 8-10 cm. Other segmental perforators from intercostal and lumbar vessels also perfuse this muscle. The nerve supply is by thoracodorsal nerve from the posterior cord of the brachial plexus. This muscle arises from T7-T12 thoracolumbar spine, posterior iliac crest and angle of scapula and inserts in bicipital groove of humerus. Rowsel et al. studies the anatomy of subscapular-thoracodorsal axis and found 97% of subscapular artery was a branch of 3rd part of axillary artery, 94% thoracodorsal artery was a branch of subscapular artery, and 99% of thoracodorsal artery had serratus branch. Thoracodorsal artery had ~3mm diameter and was 8.4cm long.[3] Latissimus dorsi flap is a robust, workhorse flap that can cover prosthesis, is aesthetically pleasing, single-stage (if used with breast implant), recovery time is moderate, operation time is not too long and can survive on reverse flow from serratus branch. Disadvantages include need to turn patient, often requires an implant, scar on back, seroma, shoulder stiffness in athletes or manual workers (e.g. decorator) and colour match. This flap is used when reconstructing a large breast where implant alone is not sufficient, chest wall tissues are unsuitable for tissue expansion, where there is requirement of additional tissue, in partial breast reconstruction, in congenital breast hypoplasia (e.g. Poland's) and at patient's will. It is contraindicated in case of previous thoracotomies, where there is an injury to thoracodorsal vessel or muscle itself. While harvesting the flap, patient needs to turn to a lateral position. The skin paddle may be oriented in transverse, longitudinal or oblique fashion.[4] The origin can be detached to increase the reach. The muscle may be denervated to avoid muscle contraction. While closing the donor site, quilting stitches are applied to reduce the seroma or fibrin sealant or sclerosing agents may be used. During inseting, the upper and medial edge is sutured, implant is placed if needed, inframammary fold is created, and the skin paddle is tailored according to reconstruction requirements.[5]Complications include wound breakdown, expander failure, implant complications – infection, extrusion, seroma, scar, muscle twitching, shoulder girdle dysfunction and lumbar hernia.[6]

II.   TRAM (Transverse Rectus Abdominis Myocutanous Flap)

Transverse rectus abdominis myocutaneous flap is type III muscle flap based on superior epigastric and deep inferior epigastric artery and intercostal arteries and has segmental nerve supplyfrom T7-T12. It arises from the pubic crest and

inserts on 5-7 ribs. It gives good aesthetic results, usually provides enough tissue for total autologous reconstruction. There is no microsurgery involved and thus has short operative time. This option carries disadvantages of significant recovery time, is a tedious surgery, there is fullness in inferiomedial aspect from pedicle, a large amount of muscle is harvested so there are chances of abdominal hernia, poor vascularity in the peripheral zone, high rate of fat necrosis (up to 42%), reduced abdominal wall function, long recovery and costal nerve compression. It is indicated in immediate or delayed breast reconstruction, unilateral or bilateral breast reconstruction, young, athletic patients, large contralateral breast, when latissimus dorsi is not an option and in previous implant complications. Relatively contraindicated in physiologically old, obese, smokers and diabetic patients, patient with autoimmune disease, vasospastic disorders, cardiorespiratory disease, psycho-social problems, abdominal scars disrupting vascular anatomy, previous or planned radiotherapy, locally advanced breast cancer and by an inexperienced surgeon. To improve the flap survival, zone IV should be discarded, or strategical delay should be opted, anterior rectus sheath should be preserved, also by use of bipedicle muscle. Complications include partial flap loss in 8.5% of cases, haematoma, seroma, partial/total flap loss, hernias and abdominal wall laxity, fat necrosis and umbilicus necrosis.[7] Transfering this muscle as a free flap increases vascularity, more tissue is readily transferred, smaller amount of muscle is harvested, less reduced abdominal function and reduced blood loss, all 4 zones can be reliably transferred, there is no medial fullness from tunnelling flap, shorter hospitalization time, fewerchances of fat necrosis and partial flap loss and is better in smokers and the obese. This needs a high level of surgical expertise post-op complications but still have functional impairment of abdominal wall, there is increased lateral fullness, may need rib resection for anastomosis and need mesh for abdominal donor site closure. Donor site complications include haematoma, wound infection, mesh infection, asymmetry, bulging, hernia and decreased abdominal strength.[8] Main disadvantage of TRAM is that it is based on non-dominant blood supply (superior epigastric), that it violates the integrity of anterior abdominal wall muscles and leaves an unsightly bulge in epigastrium.

III.   Deep Inferior Epigestric Artery Perforator Flap(DIEAP)

DIEAP is the standard of breast reconstruction in most of Europe and USA Koshima first described the use of muscle sparing deep inferior epigestric artery perforator flap to avoid abdominal wall complications.[9]Vandevoort did a study on vascular perforator in 100 flaps and found 65% hadshort intramuscular course, 16% perforators were at tendinous intersection, 9% had long intramuscular course, 5% were subfascial, and 5% had a paramedian course.[10] Advantages of using perforator flap from abdominal wall include harvesting of only what is needed, respect of donor site anatomy and function. Like other free tissue transfer, this flap also requires a high level of surgical expertise andincreased operating time. Complications include

microsurgical problems, haematoma, total flap loss, partial flap loss (zone IV), fat necrosis and delayed healing.

The use of superficial inferior epigastric artery (SIEA) flap poses no damage to muscle or aponeurosis. There is no risk of post-operative abdominal wall weakness, is quick to harvest, and easier dissection and post-operative morbidity is comparable to abdominoplasty. SIEA is not present in 30-35%, pedicle can easily be damaged by other surgical procedures, has short pedicle length and small diameter of vessels (1.5-2mm), and has higher risk of partial or total flap necrosis. It was first described by Arnez.[11]

IV.   Common Miscellaneous Options

Many other options are available for breast reconstruction using free tissue transfer. Contralateral latissimus dorsi flap can be used as a free flap if ipsilateral muscle is not available. The lateral transverse free thigh flap hasan obvious scar and contour deformity.[12]Rubens flap or deep circumflex iliac artery (DCIA) flap without the bone is for patients who have had previous abdominoplasties or who may need a balancing procedure for other hip. This flap includes harvesting full-thickness square of abdominal wall muscle, including both obliques & transversalis muscle (need to be reattached to iliac crest afterwards). There isa high seroma rate.[13] Superior gluteal artery perforator flap gives an abundance of adipose tissue even in thin patients, has long vascular pedicle, the scar is obscure, provides an improved projection of reconstructed breast and preserves gluteus maximus muscle and its function and can be sensate but is technically demanding surgery.[14] Inferior gluteal artery perforator flap and transverse gracilis myocutaneous flap have also been described, but both have their limitations.

The gracilis myo-cutaneous flap represents a useful alternative in small-breasted patients with ample medial thigh tissue[14]. The flap can be oriented vertically or transversely, but the transverse upper gracilis flap results in a more well-concealed scar. The gracilis muscle is harvested with the overlying skin, including a perforator arising from the medial circumflex fem-oral artery, but has a shorter pedicle measuring 6 to 8 cm, with a relatively smaller artery. The length and caliber of the transverse upper gracilis pedicle is often better suited for internal mammary vessel perforators or distal internal mammary vessels to minimize the size mismatch. The amount of tis-sue harvested should allow a tension-free closure to avoid scar widening and migration[14].

For patients who have more fat distribution in the flanks, the lumbar artery perforator flap represents a reasonable option that provides soft, pliable tissue closely resembling breast tissue and also achieves a pleasing aesthetic contour in the donor site. Likely the greatest limitation of the lumbar artery perfo-rator flap is the pedicle length and caliber.

Some flaps have also demonstrated spontaneous return of sensation without a nerve repair. Nonetheless, there are studies supporting the effi-cacy of performing nerve coaptation. Flaps with a neurorrhaphy generally demonstrated supe-rior and earlier return of sensation compared to noninnervated flaps. The reinnervation can be performed directly or using a nerve graft or conduit. Further studies are needed to decipher the best technique for innervating a sen-sate breast flap, but the current literature demon-strates promising results.

What reconstruction should be opted, is multifactorial decision including appropriate patient selection, patients needs, and patients will. Women who underwent breast reconstruction with flaps from either the latissimus dorsi or the rectus abdominis had similar satisfaction scores.[15] Although a significantly decreased number of patients reported satisfaction with the appearance of the breastin case of DIEP flap almost all patients would have chosen breast reconstruction again, and the consistency of the reconstructed breast was evaluated as improved.[16] .

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Archives of Surgical Research | Systematic Literature Review

Artificial Intelligence In Breast Screening: A Systematic Literature Review

Haseeb Arif, Emaan Tindyala, Hira Ashraf

IMPORTANCE Breast cancer is the most prevalent cancer in women worldwide. Early presentation, detection and prompt treatment limit morbidity and mortality due to breast cancer. Conventionally, breast cancer screening techniques and diagnosis have relied upon interpretation of radiologists and pathologists. However, advancement in artificial intelligence can lead to further enhancement in accuracy and efficiency of these diagnostic techniques, thereby, reducing incidence of morbidity and mortality.

AIM This systemic literature review is conducted to ascertain whether artificial intelligence (AI) can be used to complement existing breast cancer screening techniques. Objective of this review is to determine whether AI can enhance sensitivity of screening techniques, enable more accurate classification of benign and malignant tumors and improve assessment of response to neoadjuvant therapy

METHODS This systemic review is conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. A comprehensive computer literature search in database of PubMed was performed using a combination of search terms: 'Artificial intelligence' OR 'AI' OR 'Machine learning' AND 'Screening' AND 'Breast cancer'. 843 articles were identified through search in PubMed database. Following removal of 4 duplicate papers, titles and abstracts of 839 articles were reviewed. 115 articles with relevant titles and abstracts were analyzed. Following thorough analysis, 15 papers were included in this literature review.

RESULTS AI algorithms exhibited capability in classifying breast lesions and identification of malignancy in otherwise suspicious lesions across different imaging techniques. The integration and assistance of AI algorithms in interpretation of MRI, mammography and thermography has led to significant improvement in diagnostic accuracy and classification of breast lesions. AI complements radiologists and aids in improving performance, thereby, generating better results. AI has the capability to predict response to neoadjuvant chemotherapy in breast cancer patients, leading to safer, more effective and more cost-effective treatment for breast cancer patients.

CONCLUSIONS Artificial intelligence has the potential to revolutionize medicine in 21st century. Artificial intelligence has widespread potential in breast cancer screening. It can aid in improving radiologists' ability to detect cancer on radiograms, classifying breast lesions, and predicting response to neoadjuvant therapy.

KEYWORDS Artificial Intelligence, Machine Learning, Neural Networks, Breast Cancer, Neoadjuvant Therapy, Screening.

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Systematic Literature Review

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author:
Dr. Hira Ashraf
Department of Surgery
Shalamar Medical & Dental College, Lahore
hiraashraf_5@hotmail.com
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Breast cancer is the second most common cause of cancer related death in women worldwide. Globally, it is one of the most common cancers in women [1]. Despite its high prevalence early detection and prompt treatment are highly effective means of limiting mortality [2]. Screening techniques such as mammography, MRI, ultrasonography and biopsy are the mainstay in breast cancer screening [3]. Advancement in technology especially in the field of artificial intelligence (AI) has led to further enhancement in accuracy and efficiency of these diagnostic methods. Implementation of artificial intelligence in breast cancer screening can potentially lead to further reduction in mortality in breast cancer patients through early diagnosis [4–6].

The concept of AI has been a subject of speculation for many decades. Alan M. Turing proposed the query about machine thinking in his 1950 paper. Turing believed that the ultimate form of AI would be indistinguishable from a human being [7,8]. Subsequent research led to the creation of IBM's Deep Blue, thereafter, marking the initiation of further advancement and implementation of AI in the field of medicine [9]. A wide range of tools have emerged from the field of AI. These tools are broadly classified into knowledge-based systems (KBS), computational intelligence (CI), and hybrids. In KBS knowledge is explicitly modelled in words and can be interpreted by a human. In CI knowledge is represented by figures. Hybrids find numerous applications in multiple fields such as agriculture,[10] education, economics, medicine and others [11]. AI has been used to

classify skin cancers with accuracy on par with certified dermatologists [11]. In addition, it has been used in intraoperative margin assessment of breast tissue to identify breast cancers [12]. A study at Children's National Medical Center in Washington, showed that a supervised autonomous robot could perform soft-tissue surgery [13].

Conventionally, breast cancer screening and diagnosis has relied upon interpretation of radiological images and biopsy specimens by radiologists or pathologists. However, significant research is being conducted so that this task can be handed over to AI for greater effectiveness [14]. Artificial intelligence is the ability possessed by sophisticated software to analyze information critically with a higher degree of efficiency [8]. Unlike a human being, it is devoid of fatigability and emotionality [15]. Deep learning is a type of AI that refers to an algorithm that uses multilayered 'neural networks' to learn information and feed it into network [16]. After sufficient learning this algorithm can be used to detect similar patterns in any new data presented to it. Deep learning convolutional neural networks contains neural networks with many layers. It has already been used in detection of breast cancer and mitosis on histological images [17].

Past research has also demonstrated that implementation of AI in the detection of breast cancer led to greater sensitivity and specificity when compared to the results produced by human professionals alone [18,19]. In this systemic literature review we seek to analyze the potential role of artificial intelligence in improving breast cancer screening in women.

METHODS:

This systemic review is conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. Objective of conducting this review is to ascertain whether artificial intelligence can be used to complement existing breast cancer screening techniques.

Search strategy: A comprehensive computer literature search in database of PubMed was performed. The search algorithm was based on a combination of keywords: 'Artificial intelligence' OR 'AI' OR 'Machine learning' AND 'Screening' AND 'Breast cancer'. All search papers were reviewed according to the selected criteria.

Inclusion of articles: Computer literature search on PubMed database using the aforementioned keywords and additional filters yielded 843 articles. Additional filters applied during search included 'Species: Human', 'Sex: Female', 'Subject: Cancer', 'Average age of participants: ≥40 year'. All articles from 1/1/2019 till 1/5/2021 were included in the search process. Clinical studies, clinical trials, randomized control trials, systemic reviews and meta-analyses were reviewed during detailed analysis. Following removal of 4 duplicate papers, titles and abstracts of remaining 839 papers were reviewed. Papers with relevant

titles and abstracts were filtered, yielding 115 papers. Full text versions of 115 papers were reviewed and 26 papers were analyzed thematically. Following detailed analysis for suitability of inclusion, 15 papers were included in this literature review. Exclusion criteria included duplicate papers, papers with irrelevant titles, papers with irrelevant abstract, papers with irrelevant themes and papers not available in English language. Article selection process is given in Diagram 1.

Data synthesis: Thematic analysis of 26 papers was done. Following evaluation of suitability for inclusion 15 papers were used in this review. Data about author name, year of origin, type of AI used, purpose of study, screening method and key findings was collected and coded. These themes identified through data analysis are given in table.

RESULTS

843 articles were identified through search in PubMed database. Following removal of 4 duplicate papers, titles and abstracts of 839 articles were reviewed. Full text versions of 115 articles with relevant titles and abstracts were thoroughly analyzed. Thematic analysis of 26 papers was done. Following detailed analysis 15 papers were included in this review. Themes identified through analysis of data are coded in table 1.

Classification of breast lesions: MRI has a high diagnostic accuracy for detecting calcified and non-calcified breast lesions [13,20,21]. Hence, application of AI to enhance this highly effective screening technique results in even greater sensitivity and accuracy. P.Herent et al, proposed a 50 layer residual neural network (ResNet-50) that used two-step system of detecting a lesion and classifying it into: normal tissue, other benign lesions, invasive ductal carcinoma (IDC), other malignant lesions and malignancy [22]. This exhibited an overall AUC (area under the curve) of 0.817 across all classifications, being particularly capable of identifying malignancy (AUC: 0.869) [22]. Another paper used a SVM (support vector machine) using machine learning to identify malignancy, achieving an AUC of 0.90, hence, accurately identifying malignant lesions [23]. However, both of these systems relied on significant pre-processing of MRI prior to interpretation by the AI algorithm. The residual neural network devised by P.Herent et al, relied on an 'attention block' which was trained to initially detect area of anomaly and feed this data to a second branch that averaged features maps over selected areas [22]. The second study involved pre-analysis of the image by a clinical post-processing platform, performed by a radiologist, which generated quantifiable characteristics of that image (i.e., lesion size, diffusion restriction, T2w signal intensity and vascularity). These characteristics served as predictors of malignancy once entered into the algorithm. This study also implemented machine learning (ML) algorithm into an open access internet application that could predict whether a lesion on

MRI image was benign or malignant, upon entering the aforementioned characteristics of MRI image. Further research is required for the validation of these algorithms with additional 3D image information and morphological data [22].

Another uncommon method of breast cancer screening called thermography relies on infrared radiation to detect breast lesions. One paper argued that the heterogeneity of the IR (infrared) signal emanating from the breast can be used to accurately detect possible lesions. It elaborated on the increased amount of heat generated by malignant lesions appreciable on the IR image. This increased amount of heat is generated due to angiogenesis, Nitric Oxide vasodilatory phenomenon, inflammation or action of estrogen in estrogen receptor positive malignancies, [23]. The study aimed to incorporate a deep learning algorithm (ResNet-50) with thermography (deep thermionics) to detect breast lesions in suspected patients. However, main obstacle faced was generation of very high dimensionality using the algorithm alone. It identified 2048 dimensions of IR image which would inevitably lead to overfitting and 'curse of dimensionality' [23]. The paper addressed this issue through use of an auto encoder reducing high dimensionality of the images. The autoencoder was trained specifically to reduce dimensionality hierarchically to lower dimension, reducing the dimensionality from 2048 to 16 compressed descriptors. This system captured the predominant features of IR images

with breast lesions, eliminating variations due to background 'noise' [23]. The 'deep thermionics' system of lesion detection yielded an accuracy of 78.16%. It was proposed as a viable adjunct to pre-existing breast cancer screening techniques such as CBE (Clinical breast exam), MRI, Mammography, USG etc. This autonomous system had no need for human annotated features but its inability at accurately detecting deeper lesions with a more inconspicuous cutaneous IR signature was noted [23].

Breast micro calcifications (MC)s exhibit a strong correlation with the type of breast lesion present. In malignant lesions MC appear more scattered, smaller in size and greater in number [24]. One paper aimed to elaborate use of a deep convolutional neural network (CNN) to classify breast MCs detected on mammography images. The research used a 5-layered deep CNN architecture to identify MC descriptors. This was compared to lesion classification using traditional manually extracted MC descriptors (e.g., shape, texture and morphology). It was concluded that CNN generated MC features were more accurate in classifying lesions (CNN accuracy: 0.8768 VS Manual features accuracy: 0.8667). It was also verified that traditional morphological features could be useful in guiding artificial neural network (CNN) to achieve higher accuracy for classification of MCs. CNN features filtered by morphological features achieved the greatest accuracy of 0.8859 [24].
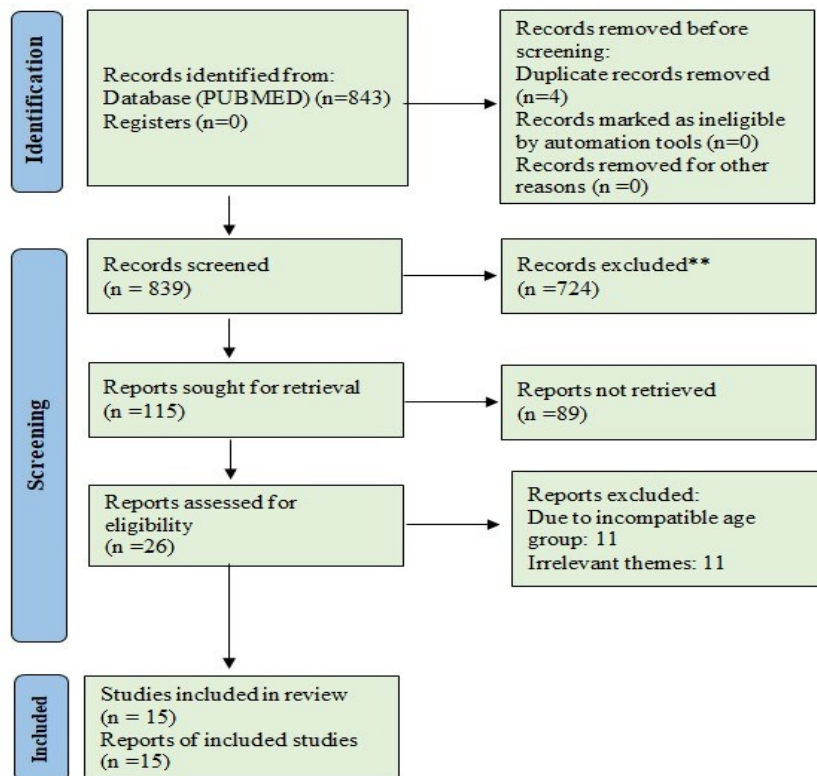
Diagram 1: Article selection process through computer literature search:

Author Name + Year of Origin	Type of AI Used	Purpose of Study	Method of Screening	Key Findings
P. Herent, 2019	DL	Differentiate b/w benign and malignant lesions	MRI (gadolinium chelate-enhanced)	Study showed good performance of the DL system in detecting lesions on MRI
Amirhessam Tahmassebi, 2019	ML	To assess complete response to NAC	MRI	ML with breast MRI enabled early prediction of pCR to NAC as well as survival outcomes
Elizabeth Hope Cain, 2019	ML, Multivariate	To assess pCR to NAC	MRI	The ML model was able to predict pCR through pre-treatment MRI features
Hongmin Cai, 2019	DL (Deep CNN)	Classification of Calcifications on Mammograms	Mammography	CNN is capable of discriminating between malignant and benign cancers using microcalcifications
Alejandro RodriguezRuiz, 2019	DL(DNN)	Identifying normal mammograms to reduce radiologist workload	Mammography	It was found to be feasible to pre-select mammograms using AI to reduce workload with minimum error
Alyssa T Watanabe, 2019	'CmAssist' DL (AI-CAD)	To retrospectively detect missed cancers on mammography	Mammography	There was an improvement in radiologist accuracy with use of cmAssist
Alejandro RodriguezRuiz, 2019	DL (CNN)	To compare the stand-alone performance of AI with 101 radiologists in detecting breast CA	Mammography	The AI had higher AUC than most of the radiologists (61% of radiologists)
Eduardo Fleury, 2019	5 different ML models used (MLP, DT, RF, LDA, SVM)	To evaluate computable BIRADS radiomic features to classify breast masses	Ultrasonography	ML can aid in distinguishing malignant and benign lesions on ultrasound images with SVM having the highest accuracy
Ji Soo Choi, 2019	DL(CAD)	To investigate whether a CAD system improves the ability of radiologists to differentiate between malignant and benign masses on breast ultrasound (US)	Ultrasonography	Radiologists' performance improved through the use of AI, with more experienced radiologists benefitting more
Stephan Ellmann, 2020	ML, polynomial kernel function support vector machine	Accurate decision rules for the management of suspicious lesions	MRI (between with BI-RADS IV or V rating)	Use of ML to interpret MRI images led to improved decision rules for management of suspicious lesions
Qiyuan Hu, 2020	DL(CAD)	To aid Breast cancer diagnosis using mpMRI	MRI	The diagnostic performance was improved by lowering false positives and increasing positive predictive values
Michael Z Liu, 2020	CNN	To predict response to NAC	MRI	The CNN algorithm proved to be feasible to predict NAC
Thomas Schaffter, 2020	Ensemble of AI's; CEM (Challenge ensemble method)	To assess whether AI could 'meet or beat' radiologists' performance	Mammography	The CEM could not beat radiologist's performance on its own but improved performance when used to complement the radiologists' interpretation
Nan Wu, 2020	DL (DNN)	Classification of screening images	Mammography	DNN model was as accurate as human radiologists
Bardia Yousefi, 2020	'ResNet-50' (DNN)	To use Infrared heterogeneity of the breast to detect potential lesions	Thermography	The AI successfully classified the normal and abnormal subjects with an accuracy of 78.16%

Table 1 : Author name, year of origin, type of AI used, purpose of study, screening method and key findings identified following thorough analysis of 15 included papers: **Important terms**: ML: Machine learning, DL: Deep learning, AI: Artificial intelligence, MRI: Magnetic resonance imaging, BI-RADS: Breast imaging reporting and data system, NAC: Neoadjuvant chemotherapy, PCR: Pathological complete response, CNN: Convolutional neural network, DNN: deep neural network, CAD: computer aided diagnosis, MLP: Multilayer perceptron, DT: Decision tree, RF: Random Forest, LDA: Linear discriminant analysis, SVM: Support vector machine, AUC: area under the curve

AI complementing radiologists and reducing workload:
Many papers have sought to evaluate performance of AI in aiding radiologists for detection of breast cancer on mammograms. 'DM DREAM', concluded that superior results were achieved when AI was used to complement radiologists' interpretation. The 8 finalist algorithms from this challenge were aggregated to increase effectiveness and performance thus forming the CEM (Challenge ensemble model). This model failed to surpass radiologists in their performance alone. However, CEM model gave

more accurate results when used to complement radiologist interpretation[15].

Another study used a deep learning AI algorithm called cmAssist to classify mammograms as 'actionable' or 'non-actionable', assigning a score to each lesion for likelihood of malignancy. 7 radiologists with different years of experience were provided the assistance of cmAssist for evaluating different mammograms. It was found that AI improved radiologists' performance by an average of 11% especially benefitting the inexperienced radiologists. It

enhanced their performance up to par with more experienced radiologists. The workload was reduced while the accuracy was increased [25]. Alejandro R-R et. al. implemented a deep convolutional neural network (dCNN) to evaluate likelihood of malignancy using a 1-10 scale. A threshold could be set anywhere along the scale to include/exclude lesions. When the threshold was set at 2 the workload reduced by 17% whereas only 1% true positive cases were missed. 2 cases were also missed by the radiologists due to their poor visibility on the mammogram [26].

AI shows promising results when used with ultrasonography (USG). It improves specificity and sensitivity when used to augment and improve radiologist interpretation [27,28]. Two studies aimed at improving radiologist interpretation of USG images and both showed improvement in performance of radiologists through the use of AI [27,28]. They used BIRADS lexicon to extract features from USG images to use for classification of malignant or benign lesions. One study showed that radiologists performed better with use of deep learning AI algorithm while interpreting ultrasonograms, especially benefitting experienced radiologists. 10.1% of previously misidentified benign cases were correctly identified and prevented from unnecessary biopsy [28].

Ai vs radiologists: A possibility and requirement exist for creation of a system that can interpret radiograms with accuracy on par with or greater than radiologists. Such a system can be used in areas with limited medical facilities to quickly screen for potential breast cancer lesions, double check results and provide accurate medical diagnoses. One such deep learning CNN algorithm proposed by Rodriguez R.A. et al, proved to be more accurate than majority of radiologists [29]. Performance of this AI construct in detecting breast CA on mammograms was compared with 101 radiologists having different experience levels. It was concluded; while AI could not outperform most experienced radiologists, yet its AUC was higher than 61% of the radiologists 29. Therefore, this stands as a testament to potential of AI in outperforming human professionals in breast cancer detection, an area where future iterations might substitute or replace inexperienced radiologists.

Predicting response to neoadjuvant therapy: Neo-adjuvant therapy (NAT) in cancer patients is a significant therapeutic modality that reduces cancer burden and improves prognosis. Research has shown that MRI is highly effective in assessing response to neoadjuvant therapy [30,31]. However, predicting a patient's response to therapy beforehand is important since only 30% of the patients benefit from NAT [6]. Early prediction of patients' response to therapy can therefore help use targeted treatment, minimize toxicity from ineffective therapies and reduce cost of unnecessary therapies. One study concluded that; CNN could predict response to NAC with an accuracy of 72% [6].

Tahmassebi A. et. al. used 8 different artificial intelligence machine learning models to pre-assess patient responsiveness to NAC. The study used a wide range of qualitative and quantitative features extracted from MRI images (23 features/ lesion) to ascertain responsiveness of NAC. It was concluded; 'XGBoost' ML model was most effective at detecting responsiveness. Hence, this could be used as a cheaper and more accessible alternative to other methods of ascertaining response to NAC such as Oncotype Dx [30].

Cain EH et.al, concluded that using lesser extracted features led to better AI performance. 529 features were originally extracted; however less than 8 features were chosen per image. Greatest performance was exhibited by the model using least number of extracted features (n=2) [31]. Therefore, it can be concluded that AI algorithms, especially those using lesser extracted features, show promising results in the detection of the probability of patients' NAC response. It can potentially lead to the reduction in ineffective therapies, reduced exposure to toxic medication and decreased treatment costs.

DISCUSSION

An alarming rise in breast cancer incidence necessitates the adoption of measures that can help reduce mortality and morbidity [32]. Regular screening, early presentation, timely diagnosis and prompt treatment play a crucial role in better outcomes [3,33]. Breast cancer screening and diagnosis have conventionally relied upon the interpretation of radiographs and histological specimens by radiologists and pathologists. This review is aimed towards determining whether AI can enhance the sensitivity of existing screening techniques, enable more accurate classification of benign and malignant tumors and the improve assessment of the patient's response to neoadjuvant therapy in breast cancer patients.

Most of the analyzed studies aimed at assessing role of AI in complementing radiologists in reducing their workload but very few were found to be assessing role of AI in evaluating response to neoadjuvant therapy and even fewer sought to develop AI that could match or outperform radiologists. It leaves much capacity for further research and development of AI that can assess patient response to neoadjuvant chemotherapy. Neoadjuvant chemotherapy is an important part of treatment for breast cancer patients, AI can help eliminate burden of unnecessary therapy and potentially prevent unnecessary exposure to highly toxic therapeutic chemotherapy. In addition, development of autonomously working AI that requires little human input can be highly beneficial in developing countries where medical facilities are limited and patients cannot afford services of qualified practitioners and radiologists.

A self-sufficient and highly sensitive AI construct can also be used in developed countries to 'Double check'

radiologists' interpretations for greater sensitivity. It can also aid in reducing the number of false positives and unnecessary biopsies. This 'double checking' is already practiced in European nations where one radiologist's diagnosis is cross checked and confirmed by another. Using a highly capable and approved AI algorithm can lead to greater sensitivity and specificity with reduced cost and workload for doctors. AI can also be used to train students more efficiently with lower costs.

Several studies have evaluated use of AI to aid radiologists in reducing their workload and increasing efficiency. As we strive to improve cancer detection several steps have been taken to improve performance and sensitivity of radiologists such as computer aided diagnosis (CAD) and double reading.   CAD has widespread implementation worldwide. Double reading as mentioned above is used in Europe where two radiologists read the same radiograph to confirm and complement on each other's findings. Research has demonstrated that the aforementioned methods are ineffective in increasing radiologist efficiency. Studies have failed to prove role of CAD in improving screening outcomes, because of the low specificity of these systems [26]. This review concludes that use of AI to complement radiologists led to superior outcomes in all of the studies. However, more research in required in field of AI. Most of the research done is centered on commonly employed screening techniques such as MRI and mammography; whereas other screening methods such as thermography are found to be underrepresented.

AI algorithms examined exhibited a good capability in classifying breast lesions and identification of malignancy in otherwise suspicious lesions across different imaging techniques. The integration and assistance of AI algorithms in the interpretation of MRI, Mammography and Thermography led to significant improvement in classification and diagnostic accuracy of breast lesions.

LIMITATIONS AND RECOMMENDATIONS
This systematic literature review is limited by use of only one database for collection of resources. It includes studies on female patients only; all studies on male patients were excluded. Owing to lack of funding it is subject to limitations of previously published data available on the used database.

In future studies, more resources can be used to further elaborate and evaluate role of AI in breast cancer screening across different countries and populations. Funded studies inclusive of all types of breast cancer in both genders should be conducted. More research is needed on evaluation of role of AI in assessing response to neoadjuvant chemotherapy. Further study is also required to evaluate significance of AI in improving less common screening techniques such as thermography and breast specific Gamma imaging.

CONCLUSION

Artificial intelligence has the potential to revolutionize medicine in 21st century. As more focus is diverted towards early diagnosis and screening of malignant conditions, for instance breast cancer, AI provides an effective avenue towards improving diagnostic capabilities and leading to lower associated mortality and morbidity.

Although there is much room for improvement and further development, use of AI in breast cancer screening has proven to be highly effective in detecting breast cancer through a wide range of screening techniques (e.g., MRI, Mammography, USG etc.). It holds the potential to complement radiologists, increasing their performance while reducing workload. AI has also shown the potential to substitute human radiologists in impoverished areas with deficient medical services, providing diagnostic capability on par with or perhaps superior to radiologists. AI can also be used to tailor and modify treatment modalities for individual patients as shown through its capability in predicting response to neoadjuvant chemotherapy in breast cancer patients, leading to safer, more efficient and more cost-effective treatment. Further research is required with greater number of subjects and adequate funding to refine and improve medical uses of AI, since it holds the potential to vastly improve field of radiology and medicine.

Author Affiliations: Department, Shalamar Medical & Dental College, Lahore, Pakistan

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Archives of Surgical Research | Pictorial Perspective

Tips And Tricks To Read A Mammogram: What A Surgeon Needs To Know

Arqam Awais[1], Muhammad Omer Altaf[2], Haroon Shahid[2]

IMPORTANCE Breast imaging is one of the most widely used radiological techniques all over the world owing to its high detection rate of early breast cancers, cost effectiveness and it being an easy to handle modality. Breast cancer is one of the most commonly occurring malignancy in women with a high mortality rate if undetected. Early effective detection has resulted in decreasing the mortality.

The most commonly available breast imaging techniques include ultrasound, mammography, MRI and nuclear techniques. Recent advancements have provided advanced results in terms of lesion detection like full field digital mammography (FFDM) and computer aided detection (Artificial Intelligence). Mammography is one of the best screening tool for breast cancer especially in asymptomatic women above the age of 40 years as demonstrated by various randomized control trials and mass screening programs. The objective of this short communication is to give a brief overview of how to read a mammogram.

KEYWORDS: Mammogram, Breast Cancer, Reading Mammogram, BIRADS Classification

Pictorial Perspective

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author:
Dr. Arqam Awais MBBS
Radiology Department,
Shaukat Khanum Hospital
Lahore arqamovais@gmail.com
092 – 333 - 4714155
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M ammography is the two-dimensional X-ray representation of breast tissue to detect breast lesion. General mammography can be categorized into two segments i.e. screening mammography and diagnostic mammography. Screening mammography target the asymptomatic women and aims to detect any breast abnormality at an early stage to reduce the incidence of advanced breast disease and thus reducing morbidity and mortality. The diagnostic mammography on the other hand focuses on differentiation of lesions to arrive at a diagnosis followed by suitable treatment method[1].

In technical aspects, there are also two types of mammograms, film screen mammography and digital mammography of FFDM; the main difference among these two is in former the image is presented and stored as radiographic films, while in latter the digital files are stored on computer for post processing.

The interpretation of mammogram has been conducted by breast surgeons in breast clinics as well. Many researches have been performed to determine the accuracy of mammography reporting by surgeons and it showed that surgeons can be involved in double reading of mammograms. The screening mammogram are performed at a larger scale and their reporting is simpler as compared to diagnostic mammograms. A mammogram has two standard views including craniocaudal (CC) and mediolateral oblique views (MLO) of each breast.

The reading of mammogram can be made easier for breast surgeons following a standard sequence and simple tricks.

STEPS TO APPROCH A MAMMOGRAM

First step should be checking for proper acquisition of the mammogram which includes procedure justification, correct exposure, proper positioning, adequate compression of breast tissue while taking images, no skin folding, imaging of the whole breast tissue, coverage of axilla and avoidance of any artifacts during the procedure. Images obtained should be symmetrical.

Second step is identification of laterality, a simple trick to identify the site is straightening the arms with the palmer aspects of both hands facing each other e.g the right hand palmer aspect faces the left hand, this represents that the right breast mammogram both standard views when seen will shows the breast starting from the right of the film and bulk of breast tissue extending away towards the left i.e the palmer aspect of right hand. Vice versa for the left.

Third step is identifying the breast composition, it is classified into 4 categories a, b, c & d[2]. This is in order of increasing breast densities. The higher the density of the breast parenchyma the lower the sensitivity of mammogram becomes and need for additional breast ultrasound[3]

Right   Left
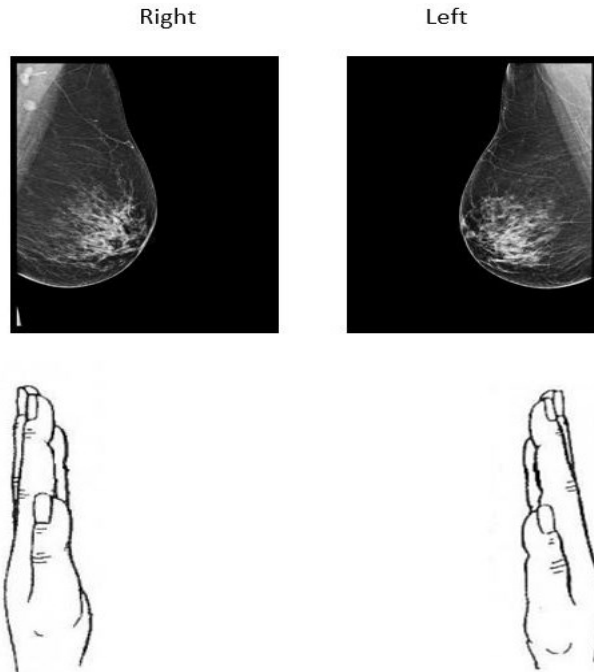
**Figure 1:** How to interpret the sides of breast on a mammogram. (*Courtesy radiologyassistant.nl [4]*)

These categories are defined by the BI-RADS area as follows:

A- The breast are almost entirely fatty.
Mammography is highly sensitive in this setting.

B- There are scattered areas of fibroglandular density.
The term density describes the degree of x-ray attenuation of breast tissue but not discrete mammographic findings.

C- The breasts are heterogeneously dense, which may obscure small masses.
Some areas in the breasts are sufficiently dense to obscure small masses.

D- The breasts are extremely dense, which lowers the sensitivity of mammography[2].
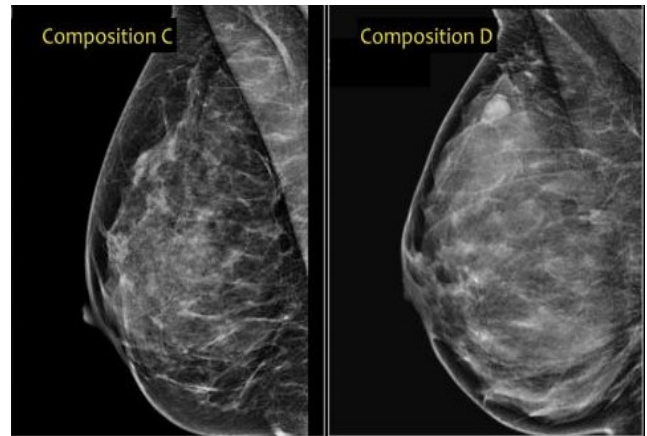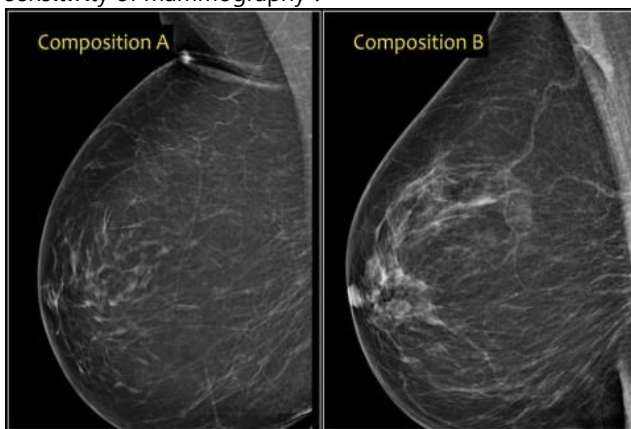
Figure 2: The figures describes the all four grades of breast density as evident on a mammogram (*Courtesy radiologyassistant.nl [5]*).

Fourth step is to identify any abnormality. Any asymmetry is suspicious. The whiter the lesion the denser it is. So any high density mass should be identified. Architectural distortion is suspicious as well. Do you see any suspicious calcifications such as pleomorphic calcification? Large calcifications i.e macro calcifications are usually not concerning. Any calcifications appearing like a vessel i.e vascular calcifications are not concerning. Few examples have been depicted below:
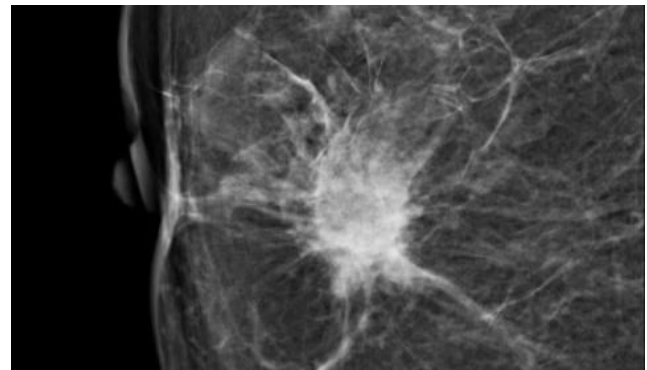
Figure 3: Hyperdense mass with an irregular shape and a spiculated margin. (*Courtesy radiologyassistant.nl [5]*)
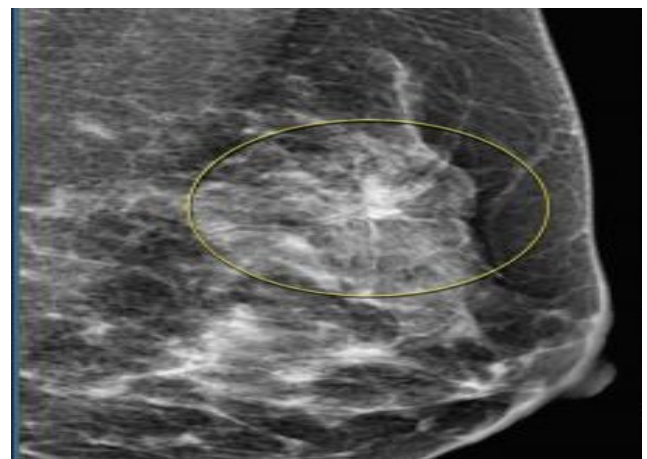
Figure 4: Focal asymmetry (*Courtesy radiologyassistant.nl*).
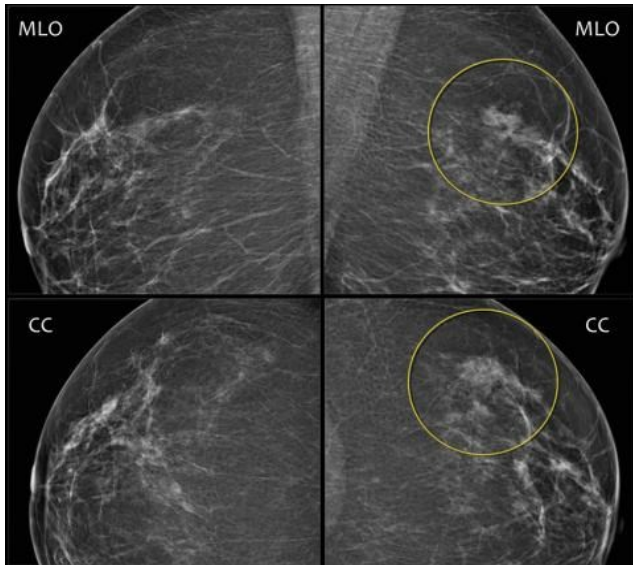
Figure 5: Architectural distortion, this is used when the normal architecture is distorted with no definite mass visible (*Courtesy radiologyassistant.nl [5]*).
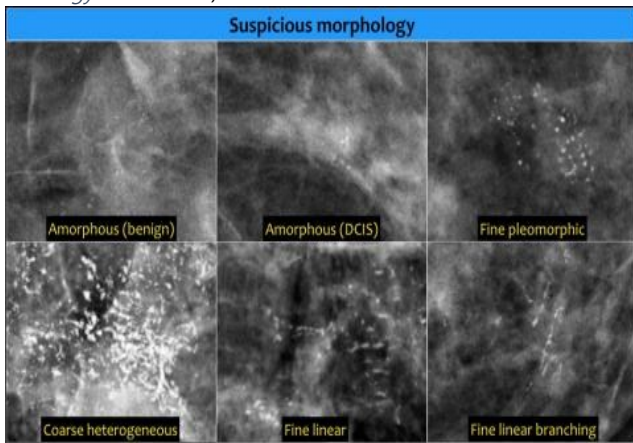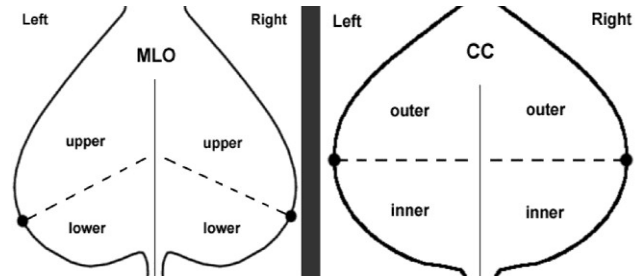

Figure 6: Multiple examples of suspicious microcalcifications (*Courtesy radiologyassistant.nl [5]*).

Fifth step is to localize the location of the abnormality in breast according to the appearance of abnormality on both views of mammogram
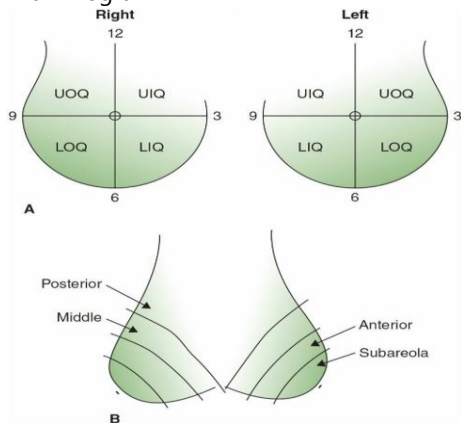
Figure 7: Breast divided into quadrants (*Courtesy radiologyassistant.nl [6]*).

Figure 8: View of quadrants on both standard views of mammogram (*Courtesy radiologyassistant.nl [5]*).

Hence if a mass is seen in the upper aspect on MLO view and outer aspect on the CC view. It will be described as breast mass in upper outer quadrant

SOME TIPS FOR SURGEONS

1. When planning of local excision surgery such as lumpectomy one can review and measure the size of lesion on the primary mammogram to get an estimate for amount of excision that needs to be done for negative margins.
2. See if there are pleomorphic calcifications associated with the mass and if the is extending beyond the mass. If it is extending beyond the mass then extended excision needs to be done in the direction where the calcifications are extending to ensure negative margins. Again measuring the abnormality on both views of mammogram can help.
3. Mammograms sometimes don't cover the inframammary skin fold (edges of breast) and axillary tail well particularly when the breast is large so it is advisable to clinically evaluate those areas or get ultrasound assessment done to avoid any concerning lesion hiding in those areas.
4. Zooming or using magnification can help to identify suspicious microcalcifications.
5. If primary breast malignancy had suspicious pleomorphic calcifications then particular attention in follow up post treatment mammograms should be made to identify these calcifications especially the surgical site to detect any early recurrence.

6. Always compare with any previous mammogram.

When in doubt or if there is any discrepancy in the clinical picture and radiographic findings never hesitate to discuss with the radiologist.

Finally the lesions are always interpreted in light of the BIRAD Classification as depicted in the Table 1.

A

B
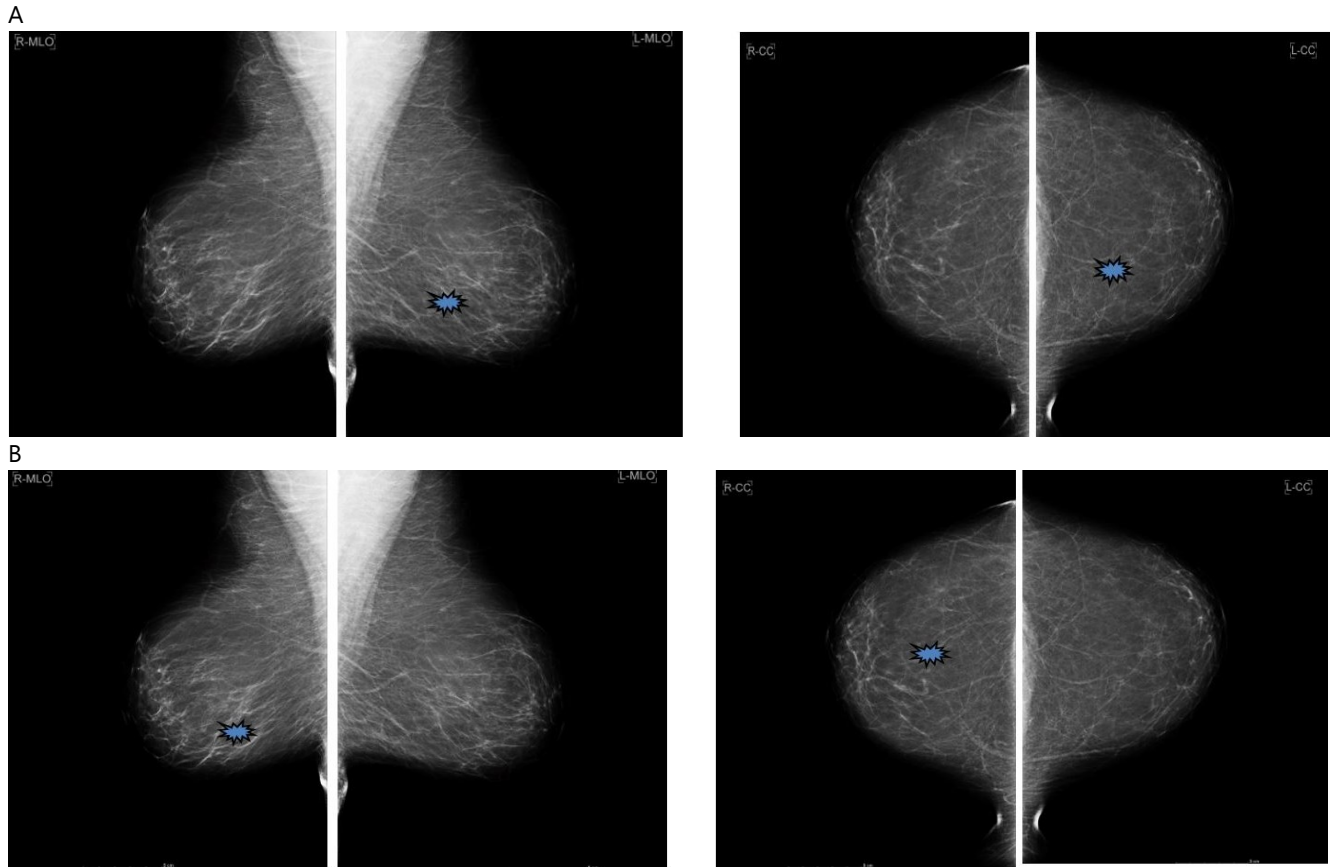
Figure 9: Practice where the lesions is: (*Courtesy radiologyassistant.nl [5]*).

Final Assessment Categories			
	Category	**Management**	**Likelihood of cancer**
0	Need additional imaging or prior examinations	Recall for additional imaging and/or await prior examinations	n/a
1	Negative	Routine screening	Essentially 0%
2	Benign	Routine screening	Essentially 0%
3	Probably Benign	Short interval-follow-up (6 month) or continued	>0 % but ≤ 2%
4	Suspicious	Tissue diagnosis	4a. low suspicion for malignancy (>2% to ≤ 10%) 4b. moderate suspicion for malignancy (>10% to ≤ 50%) 4c. high suspicion for malignancy (>50% to <95%)
5	Highly suggestive of malignancy	Tissue diagnosis	≥95%
6	Known biopsy-proven	Surgical excision when clinical appropriate	n/a

Figure 10: Breast Imaging Reporting and Data System (BI-RADS) score explained: (*Courtesy radiologyassistant.nl [5]*).

Author Affiliations: 1. Department of Radiology Shaukat Khanum Hospital Lahore, Pakistan and 2. Department of Radiology, Shalamar Medical and Dental College Lahore.

Conflicts of Interest: There are no conflicts of interest.

Disclaimer: This article does not make one eligible to report mammograms. Proper report by a certified radiologist is still mandatory.

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Archives of Surgical Research | Case Report

Congenital Eventration of Diaphragm Presenting in Adults: A Rare Clinical Scenario

Muhammad Muddassar Shafiq, Ahmad Kaleem, Talat Waseem

IMPORTANCE Eventration of diaphragm (ED) is defined as abnormal elevation of hemi-diaphragm. It may have congenital or acquired cause. Diaphragmatic eventration is rare and has incidence of <0.05%, being more common in males. A rare case of congenital diaphragmatic eventration is presented here. A 42 years old male presented with history of intermittent dyspnea and occasional epigastric discomfort. On routine physical examination, bowel sounds and decreased breath sounds were audible in left infra-axillary and left infra-scapular areas. Imaging modalities showed elevation of diaphragm, which was confirmed on CT Scan. We used thoracotomy approach for plication. Post-operatively patient suffered from left lung atelectasis for which the patient was managed conservatively. Patient was discharged after 1 week of hospital stay after having significant functional improvement.

KEY WORDS Eventration of Diaphragm, Adults, Diaphragmatic hernia, Surgical treatment

Case Report

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Mr Talat Waseem FRCS Eng, FACS, Consultant Surgeon Shalamar Medical & Dental College, Lahore twaseem@gmail.com 092-333-8078705 https://doi.org/10.48111/2021.02.11

Diaphragmatic eventration refers to an abnormal elevation of muscular part of all or portion of hemidiaphragm, without breach in its continuity, maintaining normal attachments to the sternum ribs and dorsolumbar spine.[1] It may be congenital or acquired. Acquired form has etiology of phrenic nerve injury and idiopathic .[2] It has incidence of 1:10,000 in adults, being more common in males, unilateral and left sided generally, with associations of anomalies like wandering spleen.[3] Diagnosis is usually incidental since patients are often asymptomatic or develop mild symptoms. In symptomatic cases, presentation can be either dyspnea, palpitations, chest pain or non-specific GI symptoms like dyspepsia.[4] Physical examination findings reflect decreased air entry in the lower part of involved hemithorax and possible resonance to percussion with audible bowel sounds in chest. Radiological diagnosis can be made on chest X-ray with incidental finding of elevated hemidiaphragm most of the time. In cases of doubt, thin section CT scan and MRI can be used. Ultrasound, fluoroscopy, and contrast GI studies can be used to check for complications.[5] Accurate and timely diagnosis and management of diaphragmatic eventration is important in preventing morbidity and mortality.[6] Plication of symptomatic diaphragmatic eventration has been shown to provide significant benefit. Plication of defect can be done using various approaches such as thoracotomy, laparotomy, thoracoscopy or laparoscopy.[7] Thoracotomy approach has had reported improved rates of pulmonary function variables.[8]

CASE REPORT

A 42-year-old male presented with 2-month history of intermittent dyspnea and occasional epigastric discomfort. On routine physical examination, bowel sounds, and decreased breath sounds were audible in left infra-axillary and left infra-scapular areas. Right sided chest examination was unremarkable. Rest of his clinical examination was unremarkable. On X-ray chest, raised dome of diaphragm with regular contours and bowel loops were seen on left side, and mediastinal shift was seen towards right side. There was no blunting of costophrenic angles. The patient had no history of any congenital anomaly or any prolonged hospital admission in childhood especially with worsening dyspnea He had no history of thoracoabdominal trauma, cardiac, head and neck surgery, neoplasm, orthopedic procedure fever and myalgias with anorexia. There was no history of pain on back of neck with tingling numbness or weakness of upper limbs and fever. He had no history of neck trauma, surgery, orthopedic intervention radiotherapy to neck, anesthesia to neck or orthopedic procedures to neck and shoulder. He had no history of recurrent cough with sputum or any catheter insertion in neck and chest. Rest of his systemic history was unremarkable. The patient had undergone admission to a public hospital on account of worsening dyspnea and was managed conservatively two months before coming to us. He had complaints of dyspepsia as well. We did a CT chest on this patient which confirmed diagnosis of eventration of diaphragm with no

evidence of diaphragmatic hernia. His routine laboratory tests were unremarkable. His ABG's revealed respiratory acidosis. His Pulmonary function tests reflected a moderate restrictive pattern with FEV1 being 61 % of predicted and FVC being 63% of predicted. Plication of left dome of diaphragm was done through thoracotomy approach under general anesthesia. We did double layered plication with running prolene sutures in first layer strengthened by interrupted non-absorbable pledgeted sutures in second layer. Patient was monitored post-operatively in ICU. Post-operatively chest X-ray showed left diaphragm at normal anatomical position. However, mild basal atelectasis of left lung was seen and managed with deep breathing exercises and incentive spirometry. Patient was successfully discharged after 1 week of hospital stay. Patient is on regular follow-up and has functionally improved.
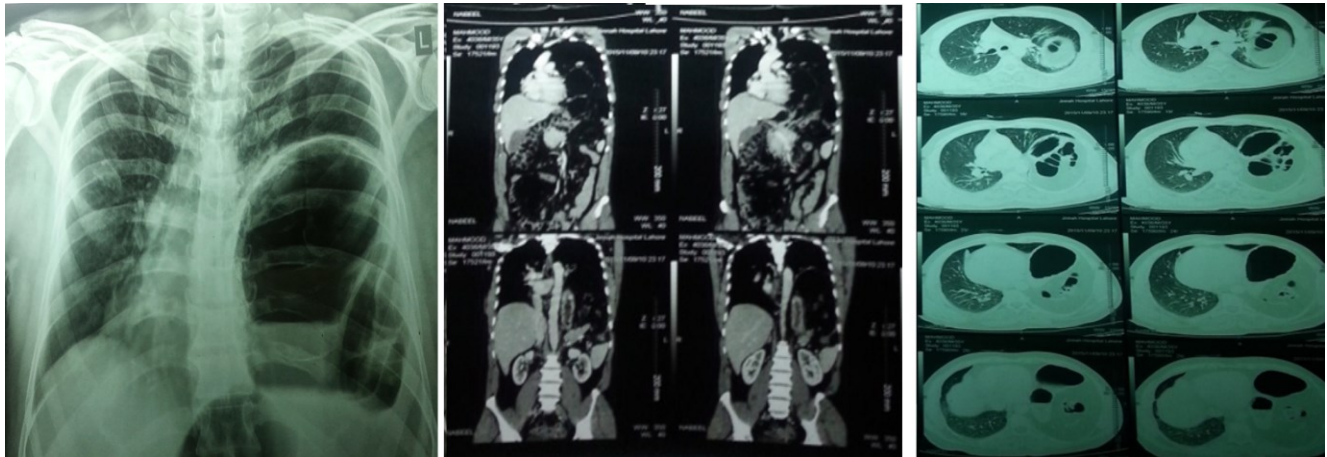

Figure 1: X-ray Chest and CT scan showing eventration of diaphragm. The affected hemidiaphragm is elevated in the shown chest X-ray with regular contours and no blunting of costophrenic angles. Atelectasis, mediastinal deviation, and bowel loops can be observed.
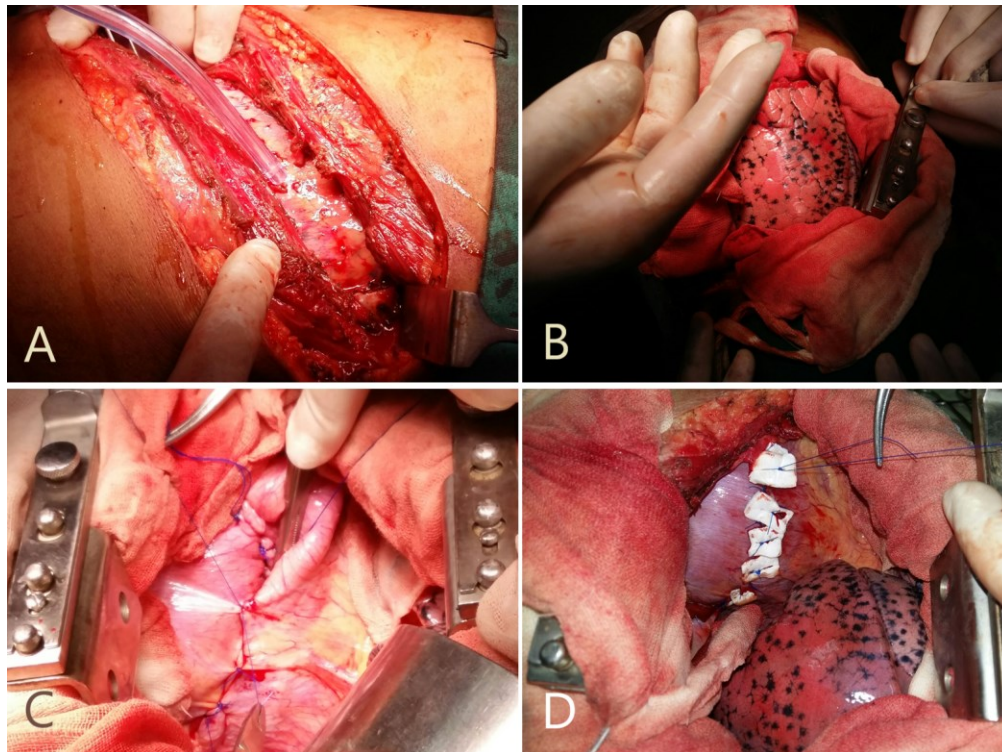
Figure 2: Postero-lateral Thoracotomy (A), Exposed Lung Parenchyma (B), Diaphragmatic Repair with running sutures (C) which have been reinforced by pledgeted sutures (D).
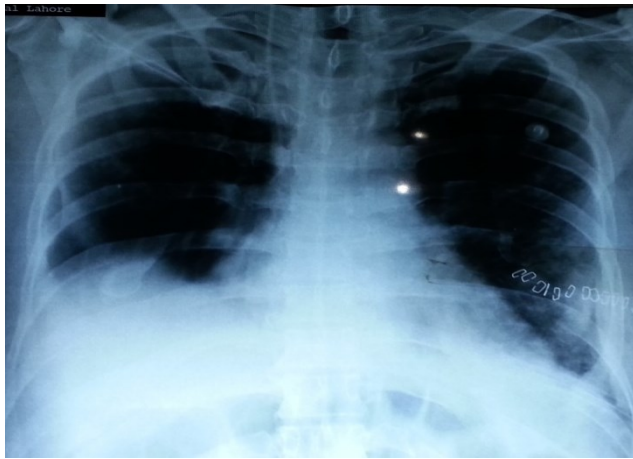
Figure 3: Postoperative Chest X-ray following repair for Diaphragmatic Eventration

DISCUSSION

Diaphragmatic eventration in its spectrum being congenital or acquired has reported incidence of <0.05% with male preponderance. The presentation range varies from asymptomatic, minimal symptoms to life threatening features with predominantly respiratory and GI complaints.[9] They have had reported genetic associations with Poland and wandering spleen syndromes [10] The symptomatology with advancing age correlates with constipation, increased stiffness of chest wall and changes in heart and lungs. On the whole, factors which push the diaphragm further up into the thoracic cavity worsen the symptoms.[11] Unilateral diaphragmatic dysfunction can compromise ventilatory function by 25% and if dyspnea which is the most common complaint progresses, it warrants plication of diaphragm to preclude worsening respiratory function.[12]

It is important to delineate symptomatic diaphragmatic eventration from diaphragmatic hernia with and without defect, because congenital diaphragmatic eventration and hernia without defect although have similar outcomes and better survival rates than the patients with a hernia having a true defect, the duration of oxygen supplementation at 30 days and recurrence rates are higher in the former group.[13] This could be due to increased utilization of multiple techniques from open to minimally invasive with varied plication patterns depending upon surgeon expertise. If the eventration is asymptomatic, we can adopt a wait and see policy. If the symptoms are present and diagnosis is established clinically , radiologically and by functional tests like ultrasound, and fluoroscopy, a period of observation of 6-12 months can be carried out before surgical plication by open or minimally invasive technique is deemed necessary.[14] Classic plication of eventration with posterolateral thoracotomy is a safe option and caters for the concept of keeping diaphragm as taut as possible which is not accurately possible with the minimum invasive techniques in which the tactile feedback is less.15 Out of multiple techniques used to make the diaphragm tight , accordion technique and double breasting technique have been commonly used. The basic idea is to improve pulmonary function and produce better patient outcomes.[16]

CONCLUSION

To conclude, congenital diaphragmatic eventration is a rare occurrence but can be deadly if it remains undiagnosed. Therefore, high index of suspicion is required while interpreting symptomatology and evaluating extremely valuable chest x rays to give us the right direction for diagnosing such diagnostic dilemmas. A simple plication can indeed save lives in diaphragmatic eventration patients.

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complete journal-specific author and conflict of interest disclosures. When submitting a group author manuscript, the corresponding author should clearly indicate the preferred citation and should clearly identify all individual authors as well as the group name. Other members of the group should be listed in the acknowledgements. In case of suspicion of gift authorship the journal may refuse further processing of the manuscript. Manuscripts with more than *Eight* authors will not be accepted for further processing and will be rejected. An author (or employer or institution) has certain rights to reuse work that this journal will not infringe upon.

Registration of Research and Clinical Trials

All types of research studies and clinical trials involving human participants should be preferably registered prior to submission, and proof of registration must be provided. Unregistered trials and studies may not be published.

Role of Funding Source

The funding source must be disclosed along with their degree of involvement with the research matter, if any, in the design, collection, analysis or interpretation of data; in the writing of the article, or in the decision to submit the article for publication. If the funding source had no involvement, then this should be stated. Any authors found guilty of scientific misconduct will be blacklisted from future publications.

4.   PREPARATION

Reviewing Process

This journal is reviewed using a *double blind* method through OJS. The following categories the journal will accept, out of guest editorials, original articles, review articles, case reports, clinical updates, short communications, book reviews, case studies, clinical notes, Continuation of Medical Education (CME), obituaries , letters, Knowledge-Attitude-Practice (KAP) studies, routine surveys and cross sectional studies. The authors are required to suggest potential refrees for the review process. The journal however would have to discretion to get the article reviewed by the suggested faculty or not.

Reporting Guidelines

Compliance with the relevant reporting guideline is mandatory for submission of the following guidelines:

1. Submit a completed checklist, indicating the page numbers where compliance to the guidelines was ensured.

2. Mention in the 'Methods' section that the research is being reported in line with the relevant guideline, which should be named and cited.

Randomized Controlled Trials

All randomized controlled trials submitted for publication in Archives of Surgical Research must include a completed

Consolidated Standards of Reporting Trials (CONSORT) flow-chart and ensure that all features of the CONSORT checklist are present. A copy of the CONSORT checklist must be uploaded in supplemental material. Refer to the CONSORT statement website here.

Systematic Reviews

Systematic reviews are to be reported in accordance to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Guidelines and must include the flow-chart as a figure and the checklist as a supplemental material. Please download a PRISMA Flowchart and a PRISMA Checklist here. To aid and improve the methodological quality of your article, include an AMSTAR 2 checklist as well, which is available here.

Cohort, Case-control and Cross-sectional studies

Cohort, Case-control and Cross-sectional studies must be compliant with the STROCSS criteria (Strengthening the reporting of cohort studies in surgery), which is available here. Cite the following paper: Agha RA, Abdall-Razak A, Crossley E, Dowlut N, Iosifidis C, Mathew G, for the STROCSS Group. STROCSS 2019 Guideline: Strengthening The Reporting Of Cohort Studies in Surgery. Each study type has its own checklist which must be uploaded as supplemental material.

Diagnostic, Quality Improvement and Qualitative studies

Diagnostic studies should be reported according to the STARD statement criteria (Standards for the Reporting of Diagnostic Accuracy studies). The flow-chart should be a figure and checklist should be uploaded as supplementary material. Quality Improvement studies must comply with the Standards for Quality Improvement Reporting Excellence (SQUIRE) criteria, which is available here. Qualitative studies require the Consolidated criteria for Reporting Qualitative Research (COREQ) checklist, available here.

Health Economic Evaluation

Health Economic Evaluation studies should conform to the CHEERS statement, available here.

Tumour Marker Prognostic Study

Tumor Marker Prognostic studies should be reported according to the REMARK criteria.

Before and After Studies

Before and After studies measure specific characteristics of a population or group of individuals after an event or intervention, compare them with those characteristics before the event or intervention, then measure the effects of the event or intervention. These studies should conform to the STROCSS statement.

Experimental Animal Studies

Animal studies must be reported according to the ARRIVE guidelines (Animals in Research: Reporting In Vivo Experiments) and must include the checklist as supplemental material. An example of a completed checklist can be found here. The institutional protocol number must be included at the end of the abstract.

Qualitative Surveys

Qualitative Surveys should be reported according to the criteria detailed in the SRQR Guidelines. Guidelines for synthesis of qualitative research can be found here. Guidelines for interviews and focus groups are available here.

Case Series

Ensure that the case series is compliant with the PROCESS Guidelines and submit a completed PROCESS checklist. State that the work has been reported in line with the PROCESS criteria and cite the following paper: Riaz A. Agha, Mimi R.Borrelli, Reem Farwana, Kiron Koshy, Alex Fowler, Dennis P. Orgill, for the PROCESS Group. The PROCESS 2018 Statement: Updating Consensus Preferred Reporting Of CasE Series in Surgery (PROCESS) Guidelines.

Article Structure

Title Page

The title page should give the title in capital letters and a shorter running title. Avoid abbreviations and formulae if possible. In addition, the title page should also include:

- Correctly spelled names of all authors, and their affiliation addresses where the actual work was done. Include the e-mail address of each author.

- Signpost clearly the correspondence author who will maintain contact at all steps of reviewing and publication, and post-publication, and answer any questions about the research. All information must be updated in case of any changes.

- Present/permanent address of every author.

- The source of funding of the research.

- The number of figures and tables, the total word count and the total number of pages of the manuscript.

- A sample Title Page has been uploaded on this page above.

Abstract

All original articles must accompany a structured abstract of up *to 250-350* words. It should state aims of the study, methodology and materials used, results obtained, and conclusions reached. Specify how the sample selection of study subjects or experimental animals was carried out, specify the observational and analytical methods, and give specific data and its statistical significance, where possible. Highlight novel and significant aspects of the study. Avoid references, but if necessary, cite the author(s) and year(s). Avoid non-standard or uncommon abbreviations, but if necessary they must be defined at their first mention in the abstract. This page should constitute of the abstract and keywords only.

Keywords

Right after the abstract, provide a maximum of 6 keywords, using British spelling. Avoid general and plural terms and

multiple concepts (avoid, for example, 'and', 'of'). Only abbreviations firmly established in the field may be appropriate. These keywords will be used to aid the indexing process of the journal.

Introduction

Outline the aims of the work and provide sufficient background information, avoiding a lengthy literature review or a summary of the results.

Methodology

Provide adequate details to allow the research to be reproduced by an independent researcher. If experimental apparatus is used, the manufacturer's name and address should be included in parentheses. Methods that have previously been published should be summarized, and signposted by a reference. If quoting directly from a previously published method, use quotation marks and cite the source. Any alterations to existing methods should also be described. If a drug is used, its common name, dose and route of administration must be included. For patients, age and sex with mean age ± standard deviation must be given where relevant to the data. Statistical methods employed for comparisons of data sets must be mentioned and any computer programs used for calculations must be specified.

Results

Results should be clear and succinct. They must be presented in the form of text, tables and illustrations. The content of the tables should not be repeated in the text; the tables should be numbered and identified and referenced to as their number. A conclusion that either supports or negates the hypothesis should be included. If the data is inconclusive, that should also be noted.

Discussions

This should emphasize present findings of the research, and the differences and similarities with prior work done in the field by other researchers. Data must not be repeated in the discussion, and lengthy citations and reviews must be avoided. Highlight the original and central aspects of the study and the conclusions that they lead to.

References

Please make sure that Mendley or some other software is used for referencing. The articles without compliance in this area would be sent back. **American Medical Association (AMA Referencing Style) should be used.** References should be typed in sequential numbers in superscript for in-text citations, and numbered sequentially in the Reference List provided at the end. Maximum references for original article should not exceed 40; they should not exceed 10 for case reports, and 80 for reviews. Authors should ensure that locally published studies are given precedence. Add DOI number of documents where it is available.

References from books should include author, title, publisher, and year of publication. Example:

Das JC. *Power System Harmonics and Passive Filter Designs*. John Wiley & Sons, Inc; 2015.

For articles in journals, the authors, title of article, name of journal, year of publication, and an article identifier and page range (where available) must be included. See the following example:

Zhu Z, Hoffman JE. Condensed-matter physics: Catching relativistic electrons. *Nature*. 2014;513(7518):319-320.

Websites that are blogs and subject to changes by the author must be used as sparingly as possible, and when included, the author's name, the title, the name of website, date of publication, date on which the website was accessed, and a link to the website must all be included. Example:

Andrew E. After Years Of Conflict, Huge Project Could Help Scientists Decipher The Brain. IFLScience. Published June 18, 2015. Accessed October 30, 2018. https://www.iflscience.com/brain/after-years-conflict-huge-project-could-help-scientists-decipher-brain/

For government reports, technical reports, and scientific reports, if the report number is unavailable, then cite the report as a book. For reports it is usually not individual people that are credited as authors, but a governmental department or agency. Include the name of the agency, the title of the report, the publisher, and the year of publication. An example is as follows:

Government Accountability Office. *The Manager, the Government, and the Accounting Profession*. U.S. Government Printing Office; 1968.

References to Ph.D. dissertations, Master's theses or Bachelor theses follow the format outlined below, and must include author, title, publication detail if applicable, and year of publication.

Campbell AJ. History transformed: Sengoku Daimyo in Japanese popular media. Published online 2012.

For newspaper articles, citation must include the author, title, name of newspaper, full date and page number. The example is as follows:

Kinsley M. Paid Leave Counts as Progress. *New York Times*. May 27, 2017:SR3

Avoid referencing personal communications and unpublished observations, but they must be presented in parentheses in the text if included, and not in the list of references in the appendix. A research article may not be cited as "Under Publication" or "In Press" unless it has been accepted for publication. In such a case, the name of the journal must be given.

Acknowledgements

All contributors who do not meet the criteria for authorship should be credited in this section. It should include persons who provided technical help, writing assistance and general support or supervision. Financial and material assistance must also be credited. Persons who have added to the material but do not justify authorship can be listed as "clinical investigators", "participating investigators", "scientific advisors", "reviewers', or "data collectors."

5.   FURTHER CONSIDERATIONS

World Limits

Maximum length of the original manuscript should not exceed *4000* words including title page, table and references. For review articles, the maximum word count is *3500,* however considering the demand of the subject it can be up to 8000 words. Maximum number of tables & illustrations should not exceed 5. Short reports of cases, clinical experience, drug trials and their adverse effects can be submitted. Maximum length of these case reports should not exceed *800* words, *5* maximum number of references, and *2* table or illustrations. For letters, maximum words are *600* with *5* references. Extra charges will be applicable for lengthy manuscripts.

Units, Abbreviations and Formulae

Système Internationale (SI) units should be used, with the traditional equivalent in parentheses where appropriate. Avoid non-standard or uncommon abbreviations, but if necessary they must be defined at their first mention. Submit math equations as editable text. Add simple formulae in line with normal text where possible and use the solidus (/) instead of a horizontal line for small fractional terms, e.g., X/Y. Variables are to be written in italics. Powers of e should be denoted by exp. Any equations that have been presented separately from the text (if referred to explicitly) must be numbered consecutively.

Artwork

Make sure to use uniform lettering and sizing of original artwork. For original illustrations, use Arial, Courier, Times New Roman, Symbol, or a font that looks similar. Number the illustrations according to their order in the text with a logical naming convention for the artwork files. Provide captions to illustrations separately. Size the illustrations close to the desired dimensions of the published version, avoiding any files that are disproportionately large. Submit each illustration as a separate file. If the electronic artwork is created in a Microsoft Office application (Word, PowerPoint, Excel) then please supply in the native document format without alterations or conversions. If the application used is not part of Microsoft Office, convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

- EPS (or PDF): Vector drawings, make sure to embed fonts.

- TIFF (or JPEG): Color or gray-scale photographs (halftones); ensure a minimum of 300 dpi.

- TIFF (or JPEG): Bitmapped (pure black & white pixels) line drawings; ensure a minimum of 1000 dpi.

- TIFF (or JPEG): For combinations of bitmapped line/half-tone (color or gray-scale), ensure a minimum of 500 dpi.

Do not supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); these typically have a low number of pixels and limited set of colors. Do not supply files that are too low in resolution. Ensure that each illustration has a separate caption that is not attached to the figure. A caption should comprise of a short title and a brief description of the illustration. Avoid text in the illustrations themselves but explain the symbols and abbreviations used.

Tables

Submit tables as editable text and not as images. Tables can be placed either next to the relevant text in the article, or separately at the end in an appendix. Number tables consecutively according to their sequence in the text and present any table notes below the table body. Keep the use of tables to a minimum and ensure that the data included in them is not repeated in results described elsewhere in the article. Avoid using vertical rules and shading in table cells.

Supplementary Material, Research Data, and Video

Supplementary material such as applications, images, and sound clips, can be published with the article to enhance it. Submitted supplementary items are published exactly as they are received (Excel or PowerPoint files will appear as such online). Submit this material with the manuscript and supply a concise, descriptive caption for each file. If you want share data that supports your research publication, where appropriate, interlink the data with the article. Research data refers to the results of experimentation that validate research results. To enable reproducibility and data reuse, share the software, code, models, algorithms, protocols, methods and other useful materials related to the project. If you have made your research data available in a public data repository, link the dataset directly into your article. To enable transparency, we require you to state the availability of data in your submission if your data is unavailable to access or unsuitable to post. Authors who wish to submit video files with their article are encouraged to include links to these within the body of the article. This can be done in the same way as a figure or table by referring to the video or animation content and noting in the body text where it should be placed, or separately at the end. Keep the file in one of the recommended file formats with a preferred maximum size of 150 MB per file, 1 GB in total.

6. **AFTER COMPLETION**

Proofreading

Final version of the article is sent to corresponding author for proof reading before publication. In case of changes, corrections should be sent to the editor by email.

Processing & Publication Charges

This is open access journal and journal charges Article Processing Charges (APC) of Rs 5000/- for local manuscripts and $US 100 for foreign manuscripts. Article Processing Charges are deposited at the time of submission and are non-refundable. Moreover, please also note that once accepted minimum publication charges for articles, manuscripts are Rs.4,000/- per page (in case of overseas US$ 50/- per page; Overseas US$ 50/- per page). Charges for photograph, films and illustrations are additional. Publication charges are payable in advance once the manuscript has been accepted for publication.

A fast track review system is in place upon deposition of additional processing fee (Rs. 20,000), however we do not encourage such route and should be employed only in significant circumstances. Moreover, this does not ensure that manuscript if accepted would be published on priority.

Above-mentioned charges have been waived till further notice. A small amount may be charged at the time publication during this interim period.

Waiver Request

Those who cannot pay for processing and publication can apply for waiver at the time of the submission of their article.

Ethics Committee Approval

All manuscripts involving human subjects must be accompanied with certificate of approval by the relevant institutional review body or ethics committee.

Informed Consent

While the actual signed consent forms need not be sent to the journal, all manuscripts reporting the results of experiments involving human subjects should include a statement confirming that informed consent was obtained from each subject or subject's guardian, after the experimental protocol is approved by relevant institutional body or ethics committee.

Letter of Undertaking

Manuscripts must be accompanied by letter of undertaking signed by all the authors

Printed Copy

One printed copy will be sent to the correspondence author. Authors can order additional copies at the rate of *cost*. Payment for additional copies should be sent in with the publication charges.

Submission

All manuscripts must be Word documents.

Ombudsperson

The journal's managing Editor can be contacted by authors and other personnel in case any grievances should arise by e-mail.

7.   PRIVACY POLICY

Archives of Surgical Research is committed to the protection of your personal information. The privacy policy outlined here applies only to information collected by Archives of Surgical Research through the http://www.archivessr.com/.

Information We Collect

We will request personal data from you to ascertain your individual user profile that may support all online activities allotted as an author, editorial member, or other connected role. Data like your name, postal address, e-mail address, telephone number and geographic locale are used as identifiers to permit access to certain content or to a secure

website. All personal information is treated by Archives of Surgical Research as strictly personal and confidential. Archives of Surgical Research won't disclose any personal information to third parties without your permission, unless required by law

Cookies

Cookies and log files are automatically recorded when you visit our site. These data includes some of the following information: IP address, host name, domain name, browser version and platform, date and time of requests, and downloaded or viewed files. This information is used to measure and analyze traffic and usage of the www.archivessr.com website and our digital products.

Making Changes to Your Information

When you have created an account on the http://archivessr.com, you can update your private information at any time through your account settings.

This statement may be periodically updated.

If you are concerned about how your information is stored, please contact us by email at editor@archivessr.com

8.   PUBLISHING ETHICS

Archives of Surgical Research follows the COPE Core Practices and ICMJE's *Recommendations to conduct, report, edit and publish Scholarly Work in Medical Journals*, and expected an ethical behavior from authors, reviewers and editors to follow guidelines. We also follow the Principles of Transparency circulated through WAME.

Allegations of Misconduct

Archives of Surgical Research (ASR) defines research & publication misconduct as follows:

- Plagiarism: the practice of taking someone else's work or ideas and passing them off as one's own.
- Citation manipulation: a problem when references do not contribute to the scholarly content of the article, and are included solely to increase citations.
- Data falsification/fabrication : intentional misrepresentation of research results
- Conflict of interest: a conflict of interest exists when a manuscript's or journal's author, editor, reviewer have a financial or personal relationship that may influence their intentions or bias.
- Redundant publication : when a published work (or substantial sections from a published work) is/are published more than once (in the same or another language) without adequate acknowledgment of the source/cross-referencing/justification (https://publicationethics.org/category/keywords/redundant-publication)

Any allegations of misconduct brought to the journal's attention will be dealt with immediately and seriously. ASR

will not accept articles that violate research & publication ethics, any manuscript not in compliance will be rejected.

ASR utilizes Turnitin to assess all submitted manuscripts, a plagiarism percentage upwards of 24% is unacceptable and articles not in accordance with this rule will be rejected.

In cases of citation manipulation, relevant COPE guidelines will be followed.

In case of suspected data falsification/fabrication, respective authors will be asked to clarify and explain their methods. Failure to do so will result in:

1. rejection of their submitted manuscript
2. communication of the authors' misconduct will be made to relevant institutions and regulatory bodies
3. black-listing of the authors from ASR for all future submissions

This is in accordance with COPE guidelines.

We follow the COPE Guidelines for sharing information regarding any misconduct with other journals. We also follow the COPE Retraction Guideline. We as a journal have policy to refer such cases to COPE if required.

In case of suspicion of image manipulation in a manuscript, COPE flowchart will be followed.

In cases of redundant publications, COPE flowchart will be followed.

Disclosures

All authors are required to submit a Disclosure of Interest form, which can be found here: http://www.icmje.org/disclosure-of-interest/. In case of an undisclosed conflict of interest, COPE guidelines will be followed.

Authorship

Archives of Surgical Research (ASR) follows the COPE flowchart to recognize potential authorship problems. Ghost, guest, and gifted authorship will result in rejection of submitted manuscript, in accordance with COPE guidelines.

ASR implements ICJME recommendations for what constitutes authorship of a manuscript.

ICMJE Authorship Criteria

As per ICMJE guidelines the authorship should be based on the following criteria:

1. Substantial contributions to conception & design, or acquisition of data, or analysis & interpretation of data.

2. We do not allow ghost, guest and gift authorships and if found so we follow COPE guidelines to handle such cases.
3. Drafting the article or revising it critically for important intellectual content.
4. Final approval of the version to be published. All those who meet the above three conditions are eligible to be included as Authors in the manuscript
5. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
6. When a large multicenter group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship defined above. Acquisition of funding, collection of data, general supervision of the research group does not qualify any one to be an author. All contributors who do not meet the criteria for authorship should be listed in the acknowledgment section. Those who provide technical support, writing assistance, or department chair who provided just general support should also be mentioned in acknowledgment. It is also important that all those whose names appear in acknowledgement must have given permission to be acknowledged.

ICMJE http://www.icmje.org

If a contributor does not fulfill the authorship criteria, ASR encourages listing them in the acknowledgements section. **All** authors are required to submit a Disclosure of Interest form, which can be found here: http://www.icmje.org/disclosure-of-interest/. In addition to submitting a disclosure of interest form, the manuscript must outline the specific contribution of each author. ASR Authors are also encouraged to link their ORCiD profiles.

Authorship disputes should be brought to light via email to relevant editors. They are handled through COPE Guidelines.

Complaints and Appeals

Archives of Surgical Research (ASR) follows COPE guidelines in case of appeals to the journal's editor's decisions and complaints about ASR's journal management of the peer review process.

If authors wish to file a complaint or appeal against an editorial decision, they are encouraged to email: editorial@archivessr.com, with the subject heading mentioning "COMPLAINT" or "APPEAL". We have dedicated Ombudsperson for handling such appeals.

Furthermore, Archives of Surgical Research (ASR) consults COPE guidelines if a reviewer is suspected of appropriating or mismanaging author material and may refer such cases to COPE if required.

Data and reproducibility

Archives of Surgical Research (ASR) follows ICMJE data sharing guidelines.

In case of suspected data falsification/fabrication, respective authors will be asked to clarify and explain their methods.

To Improve transparency, we encourage use of and link to international standard reporting guidelines such as those listed in the EQUATOR Network. We encourage pre-registration of clinical trials (and other study designs) in an online clinical study database before data are collected (eg, ClinicalTrials.gov). We encourage journal pre-registration and peer review of study protocols before data are collected (eg, as promoted by the Center for Open Science).

We have system of scruitiny to find such data manipulations, if found may result in:

1. Rejection of their submitted manuscript
2. Communication of the authors' misconduct will be made to relevant institutions and regulatory bodies
3. Black-listing of the authors from ASR for all future submissions

This is in accordance with COPE guidelines.

In case of suspicion of image manipulation in a manuscript, COPE flowchart will be followed.

Ethical Oversight

Archives of Surgical Research (ASR) follows COPE guidelines for ethical oversight, wherever applicable. ASR has it's own consent form for case reports, which is mandatory along with the submission of the manuscript. The consent form is adapted from BMJ Case Reports and is in line with COPE guidelines. To determine whether a study requires ethical approval or not, ASR looks to COPE guidelines.

Furthermore, ASR requires a transparency declaration from the lead author of an original study guaranteeing honesty and accuracy (as published & implemented by the BMJ and endorsed by the EQUATOR network).

Post-publication Review and Audit

If authors whose work has been accepted and/or published wish to retract/correct/revise their articles, please email: editorial@archivessr.com, with the subject heading mentioning "RETRACTION" or "CORRECTION" or "REVISION".

Conflict of Interest Policy

Adopted from Conflict of Interest in Peer-Reviewed Medical Journals which is prepared by WAME Editorial Policy and Publication Ethics Committees.

Articles would be published with statements or supporting documents declaring:

Authors' conflicts of interest

Sources of support for the work, including sponsor names along with explanations of the role of those sources if any in

study design; collection, analysis, and interpretation of data; writing of the report; the decision to submit the report for publication; or a statement declaring that the supporting source had no such involvement; and Whether the authors had access to the study data, with an explanation of the nature and extent of access, including whether access is on-going.

To support the above statements, editors may request that authors of a study sponsored by a funder with a proprietary or financial interest in the outcome sign a statement, such as "I had full access to all of the data in this study and I take complete responsibility for the integrity of the data and the accuracy of the data analysis."

Disclosure form is available from the website, which has been adapted from ICMJE Disclosure Form and should be filled at the time of acceptance of manuscript. Disclosures are also obtained whenever deemed necessary at the time of review and editorial tasks.

9. EDITORIAL POLICIES

Principles of Transparency and Best Practice in Scholarly Publishing are followed as per ICMJE guidelines. This Journal strives to adhere to the *Principles of Transparency and Best Practice in Scholarly Publishing* which could be found in the **DOAJ** Web site completely,

This Journal has established a guideline for editorial independence as delineated below. The guideline generally follows that created by the World Association of Medical Editors.

1. This Journal is operated by Pakistan Endocrine & Thyroid Surgeons Association (PETSA), which is publishing organization.
2. The Chief Editor is responsible for independent leadership of This Journal editorial operations. The General Publishing Editor reports to the Editor-in-Chief for all editorial matters.
3. The Editor-in-Chief has full authority over the content of this Journal and its related offerings. This includes summaries and comments on recent medical advances, opinions, blogs and news.
4. Content-related decisions are based on quality, importance, and value to the users of this Journal. Contributing authors, editors, This Journal staff are free to express responsible positions -even if these views are not in agreement with interests, policies or published research, editorial or commentary of PETSA.
5. This Journal actively seeks input regarding editorial matters from the physician Editors-in-Chief in an advisory capacity, as well as from the other editorial board members, internal editorial staff, and readers.
6. Editors-in-Chief of this Journal is empowered to create content and commentary free of commercial and organizational influence. All authors and editors operate without conflict of interest and all potential conflicts are disclosed (please also see Conflict of Interest Policy).

10.   PEER REVIEW POLICY

We follow ICMJE recommendations on the manuscript handling. The practice of peer review is to ensure that only good science is published. It is an objective process at the heart of good scholarly publishing and is carried out by all reputable scientific journals. Our referees play a vital role in maintaining the high standards Review Policy and all manuscripts are peer reviewed following the procedure outlined below:

Initial manuscript evaluation

The Editor first evaluates all manuscripts. It is rare, but it is possible for an exceptional manuscript to be accepted at this stage. Manuscripts rejected at this stage are insufficiently original, have serious scientific flaws, have poor grammar or English language, or are outside the aims and scope of the journal. Those that meet the minimum criteria are normally passed on to at least 2 experts for review. Most of the submitted manuscripts are reviewed except few invited or editorial content.

Type of Peer Review

Policy employs double blind reviewing, where both the referee and author remain anonymous throughout the process.

How the Referee is selected

Whenever possible, referees are matched to the paper according to their expertise and our database is constantly being updated. The referee is selected both from the editorial team and outside and depending on the author suggestions.

Referee Reports

Referees are asked to evaluate whether the manuscript: - Is original - Is methodologically sound - Follows appropriate ethical guidelines - Has results which are clearly presented and support the conclusions - Correctly references previous relevant work. This is a systematic process and works on the well-designed Peer Review Proforma. The confidentiality of the peer review is ensured. Reviewers are encouraged to report conflict of interest, ethical misconduct etc.

Language correction is not part of the peer review process, but referees may, if so wish, suggest corrections to the manuscript.

How long does the review process take?

The time required for the review process is dependent on the response of the referees. Should the referee's reports contradict one another or a report is unnecessarily delayed, a further expert opinion will be sought. The Editor's decision will be sent to the author with recommendations made by the referees, which usually includes verbatim comments by the referees. Revised manuscripts might be returned to the initial referees who may then request another revision of a manuscript.

Final Report

A final decision to accept or reject the manuscript will be sent to the author along with any recommendations made by the referees, and may include verbatim comments by the referees.

Editor's Decision is Final

Referees advise the editor, who is responsible for the final decision to accept or reject the article.

Conflict of Interest

All reviewers and editors have to declare any potential conflicts of interest if any. We follow COPE and ICMJE guidelines in this regard.

Editorial and Peer Review Processes Generally Follow these Steps:

We follow and request from authors, reviewers and editors the "ICJME Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals". Editorial reviewer policy is independent of any financial, academic or any other interest.

- When an article is submitted to Archives of Surgical Research, Editor makes the first check of submitted articles (structure, plagiarism, scientific quality).
- Article may be rejected, sent back for structural revision, or sent to at least two reviewers for peer review.
- After peer review process, articles may be rejected, sent back for revision requested by reviewers or accepted for publication.
- Revised articles by authors may be accepted, resent to reviewers, resent to authors for additional corrections/revision or rejected.
- Authors could not see reviewers' information. Editor may make authors' information available to reviewers or not.
- Accepted articles are forwarded to publishing process.
- Editor(s) may require additional materials or changes from authors during copy editing, composing, grammatical editing and/or proof reading steps.
- A fast track review system is in place upon deposition of additional processing fee (Rs. 20,000), however we do not encourage such route and should be employed only in significant circumstances. Moreover, this does not ensure that manuscript if accepted would be published on priority.
- Post-publication review and peer review is encouraged and is managed through letter to the editors.

11.   STATEMENT OF INFORMED CONSENT

We follow ICMJE and COPE Guidelines for appropriate consenting. Patient's privacy should not be breached without taking consent. In written descriptions there should not be any specifications regarding patients including names, hospital numbers, photographs or pedigrees unless the information is needed for scientific purposes and the patient allows for publication with written informed consent. It should be disclosed by authors to the patients that any identifiable material could be available on the Internet or in printed form after publication. Patient consent ought to be written and archived with the journal, the authors, or both, as settled by local rules and regulations. Applicable laws vary from territory to territory, and journals should make their own policies with legal guidance. Since a journal that archives the consent will be aware of patient identity, some journals may decide that patient confidentiality is better guarded by having the author archive the consent and instead providing the journal with a written statement that attests that they have received and archived written patient consent.

Nonessential identifying details should be omitted. Informed consent should be obtained if there is any doubt that anonymity can be maintained. For example, masking the eye region in photographs of patients is inadequate protection of anonymity. If identifying characteristics are de-identified, authors should provide assurance, and editors should so note, that such changes do not distort scientific meaning.

The requirement for informed consent should be included in the journal's instructions for authors. When informed consent has been obtained, it should be indicated in the published article.

- International Committee of Medical Journal Editors ("Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals")

12. GUIDELINE FOR REVIEWERS

Peer review in all its forms plays an important role in ensuring the integrity of the scholarly record. The process depends to a large extent on trust, and requires that everyone involved behaves responsibly and ethically. Peer reviewers play a central and critical part in the peer-review process, but too often come to the role without any guidance and unaware of their ethical obligations.

Archives of Surgical Research follows COPE Guidelines for educating the reviewers for the review process.

13. ETHICAL EDITING FOR EDITORS

Becoming an editor of Archives of Surgical Research is an exciting but daunting task, especially if you are working alone without day to day contact with editorial colleagues. This short guide aims to summarize key issues and to provide links to relevant pages of the COPE website as well as those of other organizations. We encourage the editorial team to consult COPE and ICMJE resources frequently for their training and handling of the manuscript and various editorial issues.

14. GUIDELINES FOR JOURNAL MANAGEMENT

We believe that Archives of Surgical Research serves as an important part of the scientific literature. Hence, its management should be of the highest quality and ethically sound. We follow COPE Guidelines to manage the top hierarchy in terms of conflicts of interest and ethical considerations. We also following COPE Guidelines for maintaining relationship of journal management to the Pakistan Endocrine & Thyroid Surgeons Association to ensure editorial independence. The journal editorial teams meets periodically at least biannually. The editorial team is independent of the society and is managed by a transparent process two yearly as per the ethical confines suggested by COPE, ICMJE and local guidelines.

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